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DIAGNOSIS AND MANAGEMENT OF INTRAOPERATIVE ARRHYTHMIAS

Stephen J. Thomas, MD, *Guest Editor*

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Preface

Arrhythmias, arrythmias, what's the big deal? A little lidocaine here, some beta- or calcium channel blocker there, and on rare occasion a zap or two and all will be well. This approach has its advocates. It also has cachet; it exudes the aura of supercompetent nonchalance. It is a bit flimsy in terms of physiologic and pharmacologic insight, but it certainly eliminates a lot of confusion and worry about some of the things seen on our operating room monitors. With the induction of anesthesia, patients with pre-existing arrhythmias suddenly display nary an abnormal squiggle; others when encountering the autonomic chaos sometimes associated with the anesthetic state, display bizarre runs and complexes that would test the equanimity of the most serene cardiologist.

This small volume attempts to eliminate or reduce some of this confusion by organizing and presenting in concise form an approach to arrhythmia diagnosis and treatment. The topics include the following: electrophysiology—normal (the basis of the electrocardiogram and the ST segment) and abnormal (mechanisms of arrhythmogenesis—this topic overlaps into a few articles; we know this part is hard, you forget it and you're not sure what it has to do with treating real people); etiology of arrhythmias with emphasis on the intraoperative variety; pattern recognition of the common arrhythmias. Our classification system is simple—ectopics beats, tachycardias, narrow and wide complex, and bradycardias and AV block. An article on arrhythmias frequently seen in the the pediatric age group is also included; treatment, both pharmacologic (this article is a handy compendium and is not intended as an evening's light reading) and electrical (pacing and cardioversion and defibrillation).

We hope these summaries will simplify intraoperative arrhythmia recognition and guide selection of appropriate antiarrhythmic therapy.

I thank the authors for their interest, their ability to synthesize a voluminous amount of material, their adherence (at least close) to a deadline, and their patience and fortitude in accepting the editor's "suggestions." Also thanks to Margaret Burns at W. B. Saunders for general editorial supervision and for her kind and gentle persistence in seeing the issue to completion.

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Basic Electrocardiography

Charles Leslie MacAdams, MD, R. William McIntyre, MD,† and Ian Robert Thomson, MD‡*

This article provides a theoretical basis for understanding the electrophysiology of arrhythmias and the electrocardiographic (ECG) changes of myocardial ischemia and infarction. The anatomy, blood supply, and innervation of the cardiac conduction system are described. Myocardial cellular electrophysiology is reviewed, and the mechanisms of arrhythmogenesis are introduced. The principles of electrophysiological testing are briefly reviewed. Vectorial concepts are used to explain the normal ECG and the changes caused by myocardial ischemia and infarction. Finally, the selection of appropriate ECG lead systems for diagnosis of perioperative arrhythmias and myocardial ischemia is discussed. This presentation is very brief and the interested reader is referred to several recent and definitive reviews.[9, 10, 15, 17, 24, 26, 31, 43–45, 50, 51, 54, 58]

ANATOMY OF THE CONDUCTION SYSTEM

Conduction Pathways

The sinoatrial (SA) node is superficially located at the junction of the superior vena cava and the right atrium (Fig. 1). The SA node contains cells with intrinsic pacemaker activity that initiate rhythmic cardiac electrical activity (normal sinus rhythm). The electrical impulse arising in the SA node spreads throughout the atria but may be preferentially conducted through the anterior, middle, and posterior internodal tracts, and Bachmann's bundle.[4] The impulse is conducted from the atria to the ventricles via the atrioventricular (AV) node, which is located in the right atrial endocardium, anterior to the cor-

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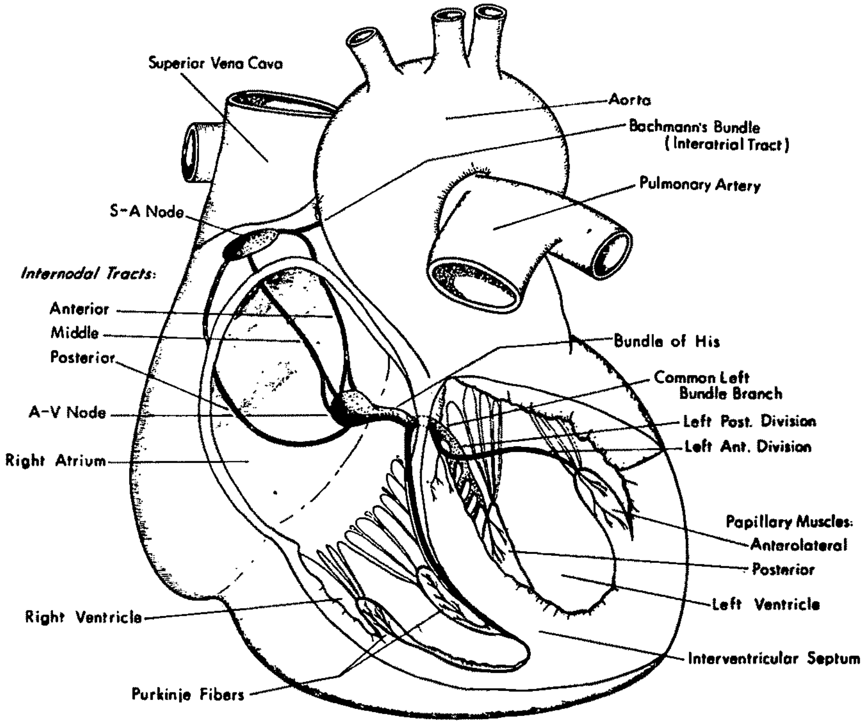


Figure 1. The cardiac conduction system. (*From* Lipman BS, Dunn M, Massie E: Clinical Electrocardiography, ed 7. Chicago, Year Book Medical, 1984, p 11; with permission.)

onary sinus ostium. The AV node contains slowly conducting cells that significantly delay transmission of the electrical impulse from the atria to the ventricles. This delay facilitates sequential atrial and ventricular contraction, which increases cardiac pumping efficiency. From the AV node the impulse is conducted by the His Purkinje system, which rapidly transmits it to the ventricular myocardium. The His bundle arises from the AV node and divides at the muscular interventricular septum into right and left bundle branches (RBB and LBB). The LBB usually divides into anterior and posterior divisions, although this is not consistent.[58] The terminal Purkinje fiber network extends from the bundle branches to the ventricular subendocardium and delivers the electrical impulse to both ventricles nearly simultaneously.

Blood Supply

The blood supply to the SA node is from the right coronary artery (RCA) in 55 per cent of patients and the left circumflex coronary artery (CCA) in 45 per cent of patients.[28] The AV node blood supply comes from the RCA in 85 to 90 percent of patients and from the CCA in the remainder. The His bundle is supplied by both the RCA and the left anterior descending (LAD) coronary artery, and so is relatively protected from ischemia.[18] The RBB and the anterior division of the LBB are supplied by the LAD, whereas the posterior division of the LBB may be supplied by either the RCA or the LAD.[36] Coronary occlusion may cause ischemia of the conduction system and blockade of impulse transmission between the atria and ventricles (AV block). Occlusion of the RCA most commonly causes conduction blockade at the AV node, whereas LAD occlusion may cause conduction blockade in the His Purkinje system (infranodal block).

Innervation

The sympathetic innervation of the heart arises from the sympathetic nerves originating in thoracic segments T1 to T4. Sympathetic effects are mediated by norepinephrine release at postganglionic nerve terminals and by circulating catecholamines. Catecholamines increase pacemaker discharge rate, shorten AV node conduction time, and decrease resistance to subsequent excitation (refractoriness), but do not affect normal His bundle conduction.[55] The vagus nerve provides the parasympathetic cardiac innervation. The effects of vagal stimulation are opposite to those of sympathetic stimulation. Parasympathetic effects are mediated by acetylcholine release and are more transient than sympathetic effects. Parasympathetic nerves exert direct effects on conduction tissue and also attenuate sympathetic activity at sites on sympathetic ganglion cells and postganglionic fibers.[20, 47] Both the SA and the AV nodes have extensive sympathetic and vagal innervation. However, the ventricles are primarily innervated by the sympathetic system, with minimal vagal supply. Right-sided autonomic nerves predominantly innervate the SA node and anterior ventricles, while left-sided nerves chiefly supply the AV node and posterior ventricles.[58] This asymmetry of innervation has therapeutic implications in long QT-interval syndromes, in which an imbalance of sympathetic tone prolongs the QT interval and predisposes to arrhythmias. A left stellate ganglion block may relieve the imbalance and prevent the arrhythmias.[19, 56]

CELLULAR ELECTROPHYSIOLOGY

Cell Membrane

Cardiac cell membranes are composed of a phospholipid bilayer in which protein molecules are embedded. The lipid bilayer is relatively impermeable to ionic species, whereas the protein structures serve as channels through which specific ions may cross the cell membrane.[31] Membrane proteins also include enzymes (for example, Na-K ATPase) and receptors for hormonal messengers.

Table 1. *Extracellular and Intracellular Ion Concentrations in Cardiac Muscle*

ION	EXTRACELLULAR CONCENTRATION (MMOL/L)	INTRACELLULAR CONCENTRATION (MMOL/L)	EI* (MV)
Na^+	145	15	+60
K^+	4	150	−94
Cl^-	120	5	−83
Ca^{+2}	2	10^{-4}†	+129

* Ei = theoretical equilibrium potential for each ion.

† Intracellular Ca^{2+} concentration represents Ca^{2+} that is not bound in mitochondria and sarcoplasmic reticulum.

(*Modified from* Sperelakis N: Origin of the cardiac resting potential. *In* Berne RM, Sperelakis N, Geiger SR (eds): Handbook of Physiology; The Cardiovascular System, ed 2. Bethesda, MD, American Physiological Society, 1979, p 193; with permission.)

Resting Membrane Potential

A microelectrode inserted into a resting myocardial cell will measure a transmembrane electrical potential of −60 to −90 mV, depending on the cell type.[50] The inside of the cell is negatively charged with respect to the outside. This resting membrane potential (RMP) results from the unequal distribution of various ions across the selectively permeable cell membrane. For example, the intracellular potassium ion concentration $[K^+]_i$ is high relative to its extracellular concentration $[K^+]_o$, whereas the opposite is true of sodium ion concentration $[Na^+]$ (Table 1). These concentration gradients are maintained primarily by the membrane Na-K ATPase, which actively pumps 3 Na^+ ions out of the cell while returning 2 K^+ ions to the cell. During the resting diastolic phase, the membrane is relatively permeable to K^+ but nearly impermeable to Na^+. Therefore, K^+ tends to diffuse out of the cell down its concentration gradient, leaving a net negative charge on intracellular anions (primarily proteins), which cannot cross the cell membrane. An equilibrium is established when the negative intracellular charge, tending to keep K^+ in the cell, equals the tendency for K^+ to diffuse out of the cell. This equilibrium can be described by the Goldman equation, which considers the concentrations of monovalent ions and their specific membrane permeabilities[23]:

$$E = -61 \log \frac{[K^+]_i P_K + [Na^+]_i P_{Na} + [Cl^-]_o P_{Cl}}{[K^+]_o P_K + [Na^+]_o P_{Na} + [Cl^-]_i P_{Cl}} \qquad (1)$$

where E = transmembrane potential (mV), $[X]_i$ = intracellular ion concentration, $[X]_o$ = extracellular ion concentration, and P_X = permeability to each ion.

Equation 1 indicates that each ionic species contributes to the membrane potential in proportion to its membrane permeability. Because the resting cell membrane is permeable only to K^+, the RMP can be approximated adequately by a simplified form of equation 1, the Nernst equation:

$$E = -61 \log \frac{[K^+]_i}{[K^+]_o} \qquad (2)$$

The Action Potential

The action potential (AP) is a self-propagating, all-or-none sequence of transmembrane potential (that is, voltage) changes caused by changes in membrane permeability to various ions, and accompanied by transmembrane ion currents. As the changes in ionic permeability are themselves initiated by membrane voltage changes, it is apparent that voltage and permeability are critically interdependent. Voltage changes likely alter permeability by affecting the conformation of protein channels in the cell membrane.[31] There are two main types of action potentials. The fast-response type is found in Purkinje fibers and working atrial and ventricular muscle. The slow-response type is characteristic of SA and AV node cells.

Fast-Response Cells

There are five distinct phases of the AP in fast-response cells (Fig. 2A). Phase 0 of the AP, rapid depolarization, is initiated when the membrane is depolarized (that is, transmembrane potential becomes less negative) to a threshold level (-70 mV for Purkinje fibers). This decrease in transmembrane potential may result from spontaneous depolarization, a propagated action potential from another cell, or an externally applied depolarizing current. Depolarization to threshold induces an abrupt increase in membrane permeability to Na^+, which then rapidly enters the cell down its concentration gradient. This Na^+ current is designated I_{Na}. Membrane permeability to K^+ falls abruptly during phase 0. These changes in permeability to Na^+ and K^+ cause the transmembrane potential to become positive (approximately $+30$ mV) and approach the equilibrium potential for Na^+. The rate of change of the membrane potential during phase 0, $\dot{V}$max, is a major determinant of impulse conduction velocity.

As the new Na^+ equilibrium potential is approached, Na^+ permeability suddenly declines and I_{Na} decreases. The abrupt decline in Na^+ permeability initiates phase 1 of the AP, early rapid repolarization to near 0 mV. Transient outward flow of K^+ and inward flow of Cl^- may occur during this phase.

During phase 2 of the AP, the plateau period, the membrane potential remains relatively stable near 0 mV, and permeability to all ions is quite low. There is a slow inward flow of Ca^{2+} ions (I_{si}) during this phase. This reflects an increase in Ca^{2+} permeability, which was initiated during phase 0. This inward Ca^{2+} flux is physiologically the most important event of phase 2 because the resulting increase in intracellular Ca^{2+} concentration $[Ca^{2+}]_i$ is essential for contraction

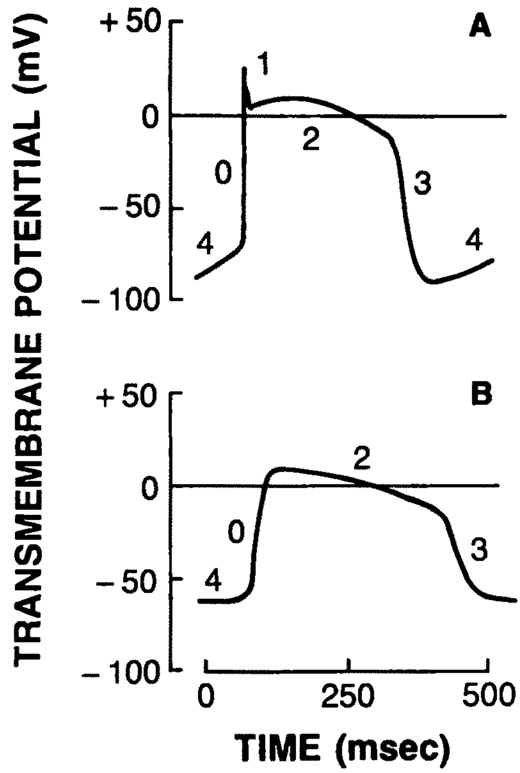


Figure 2. The two main types of cardiac action potentials. (*A*) Fast response. Phase 0, rapid depolarization; Phase 1, early rapid repolarization; Phase 2, plateau; Phase 3, final rapid repolarization; Phase 4, resting membrane potential. (*B*) Slow response. The slow response is initiated from a less negative RMP and has a less rapid phase 0 depolarization. Phase 1 is absent. (*From* Atlee JL: Perioperative Cardiac Dysrhythmias: Mechanisms, Recognition, Management. Chicago, Year Book Medical, 1985, p 27; with permission.)

of cardiac muscle. Gradual repolarization during phase 2 results from a small inward Cl^- current and Na-K exchange by ATPase.

Phase 3 of the AP, rapid repolarization, reflects a time-dependent decrease in Ca^{2+} permeability causing inactivation of I_{si}, and an increase in K^+ permeability causing activation of outward K^+ currents. This leads to restoration of the RMP (phase 4).

Slow-Response Cells

The SA and AV nodes contain slow-response cells that differ from fast-response tissue in that Na^+ channels are relatively inactive.[27] In slow-response cells phase 0 reflects inward Ca^{2+} movement (I_{si}) caused by an increase in Ca^{2+} permeability. The Ca^{2+} current is relatively slow and it is activated and inactivated more gradually than I_{Na} (Fig. 2*B*). The lower rate of depolarization, Vmax, contributes to a reduced conduction velocity in nodal tissue. Both the RMP (−50 to −60 mV) and the threshold for activation (−30 to −40 mV) are less negative in nodal tissue.

Diastolic Depolarization

In normal working atrial and ventricular muscle cells, the RMP is stable during phase 4. In contrast, in the SA and AV nodes and the

His Purkinje system, the RMP decreases spontaneously during phase 4. This spontaneous diastolic depolarization continues until threshold potential is reached, when an AP is initiated. This is called automaticity or pacemaker activity. Cardiac pacemaker cells have a voltage-dependent nonselective ion channel that is activated at membrane potentials negative to -50 to -60 mV.[14] An inward current of cations, primarily Na^+, passes via this channel and likely causes spontaneous diastolic depolarization in Purkinje fibers. In SA node pacemaker cells where RMP is less negative, this Na^+ current is less important. A decay in outward K^+ current, inward Ca^{2+} flux, and an unidentified background current likely cause spontaneous depolarization in the SA and AV nodes and partially depolarized Purkinje fibers.[35]

Normally, the spontaneous depolarization rate of the SA node exceeds that of other automatic cells, and therefore it initiates the cardiac rhythm. Other pacemaker cells are activated through the conduction system before they can spontaneously depolarize to threshold. The rate of SA node discharge is affected by changes in the RMP, threshold potential, or rate of spontaneous phase 4 depolarization. Vagally induced decreases in heart rate are probably mediated by increased K^+ permeability, which increases the RMP.[58] Sympathetically induced increases in heart rate are likely affected by decreased K^+ permeability during phase 4, leading to a more rapid decay in the outward K^+ current and more rapid spontaneous depolarization.[55]

Refractoriness

During and following an AP, myocardial cells are unable to respond to a subsequent depolarizing stimulus with another AP for an interval termed the refractory period. During the absolute refractory period, a depolarizing stimulus, regardless of intensity, cannot initiate a new AP, whereas during the relative refractory period, a larger than normal stimulus may initiate a new AP.

Propagation Conduction Velocity

The AP is propagated throughout the myocardium by sequential depolarization to threshold potential of adjacent membrane segments. In fast-response cells the primary determinant of conduction velocity, Vmax, is influenced significantly by changes in RMP and effects on the voltage-dependent Na^+ channel. When RMP becomes more negative, conduction velocity is increased, whereas when RMP becomes less negative, conduction velocity is decreased. Injury tends to decrease $[K^+]_i$ by a mechanism that remains unclear, leading to a less negative RMP.[8] This alteration tends to inactivate Na^+ channels so that less are available for the next phase 0, thus decreasing Vmax. In injured tissue, phase 0 of the AP may primarily reflect increasing Ca^{2+} permeability and I_{si}. This "depressed fast-response" may be indistinguishable from a normal slow-response AP. Decreased conduction velocity in injured cells predisposes to arrhythmias.

MECHANISMS OF ARRHYTHMOGENESIS

Arrhythmias may be caused by abnormal impulse formation (automaticity), abnormal conduction (re-entry and block), or triggered activity. An arrhythmia may be initiated by one mechanism and sustained by another. As pointed out by Rosen, it is often impossible to discern the mechanism responsible for a particular arrhythmia.[42, 43]

Disorders of Automaticity

These include sinus bradycardia and rhythms initiated by pacemaker activity outside the SA node. Arrhythmias related to SA node dysfunction may occur when altered autonomic input, ischemia, or drug effects alter either SA node discharge rate or conduction within or out of the SA node.[58] Tissues with intrinsic but latent pacemaker activity (for example, AV node, His bundle) may initiate "escape" rhythms when SA node discharge slows inappropriately or impulse conduction is blocked.

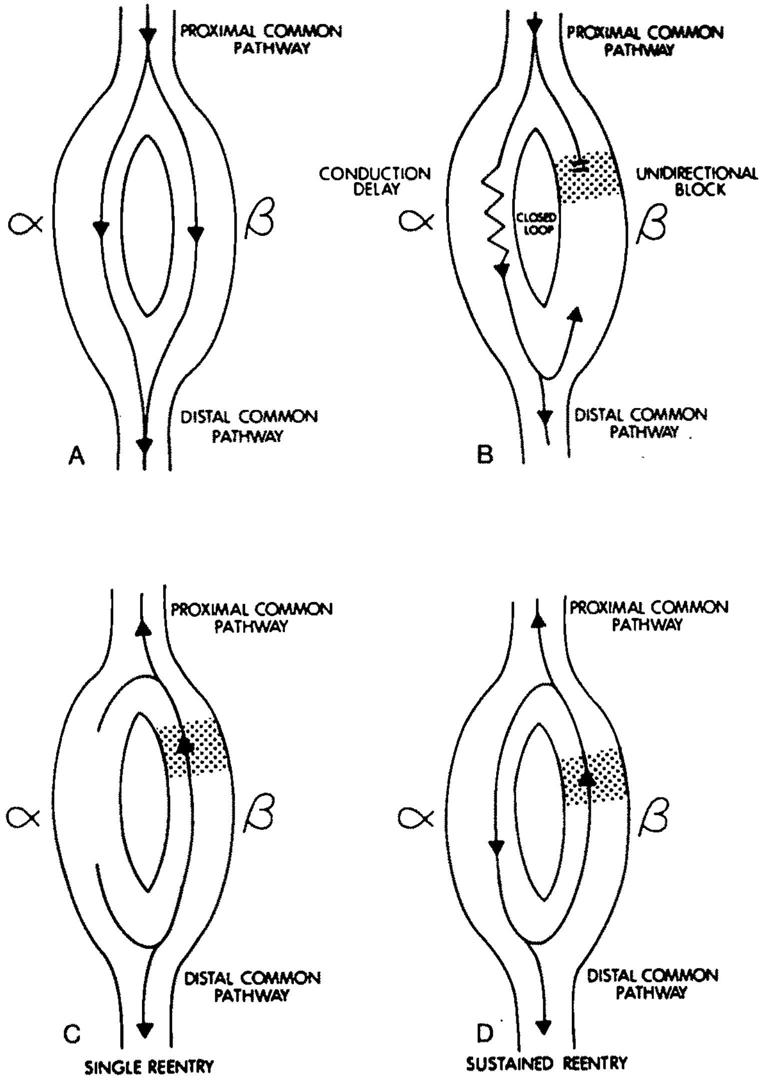
Under pathologic circumstances, latent pacemakers may dominate cardiac rhythm by discharging more frequently than the normal SA node (for example, AV-nodal tachycardia). Injured cells that do not normally exhibit automaticity also may develop spontaneous phase 4 depolarization and discharge more frequently than the SA node. This mechanism may underlie some atrial tachycardias and, less frequently, ventricular tachycardia. Experimental evidence suggests that tachycardias of more than 200 beats per minute are not caused by abnormal automaticity.[25]

Parasystole is a unique example of abnormal automaticity in which there are two cardiac pacemakers, the SA node and a second focus elsewhere in the heart. The parasystolic focus must be protected from incoming electrical stimuli (that is, entrance block), so that it will continue to discharge at its intrinsic rate. When the parasystolic discharge finds adjacent myocardium excitable, then an ectopic beat occurs. Parasystole can be diagnosed when ectopic beats occur at intervals that are multiples of the discharge interval of a hypothetical parasystolic focus that is not influenced by the SA node discharge rate. The interaction between a parasystolic focus and normal sinus rhythm may be extremely complex.[43]

Re-entry

This type of arrhythmia is initiated when circular conduction arises in a re-entry loop (Fig. 3). Re-entry requires that unidirectional conduction blockade be present in one arm of the loop. A descending impulse is blocked in this limb (the beta pathway), but is conducted with delay in the other limb (the alpha pathway). The beta pathway is then excited in a retrograde fashion. This circular impulse may be conducted to adjacent normal fibers that are no longer refractory, thus initiating a premature beat. If conduction in the loop is sustained, a tachyarrhythmia may result. Unidirectional block and re-entry may occur whenever conducting tissues with differing electrophysiologic properties form a circuit. The tissues may differ in refractory period, excitability, or conduction velocity.

Mines[39] established criteria for the proof of re-entry as the etiologic mechanism of an arrhythmia: (1) an area of unidirectional block;



SINGLE REENTRY

SUSTAINED REENTRY

Figure 3. Mechanism of re-entry. A hypothetical re-entry circuit is shown in which a proximal common pathway divides into an alpha and a beta pathway and then is reconstituted as a distal common pathway. (*A*) Normally, conduction proceeds equally in both the alpha and beta pathways. (*B*) A premature impulse encounters conduction delay in the alpha pathway, and unidirectional blockade in the beta pathway. (*C*) The impulse is conducted in a retrograde fashion up the beta pathway and past the site of unidirectional blockade, re-exciting the proximal common pathway. (*D*) The re-entry pattern is sustained facilitating a tachyarrhythmia. (*From* Gallagher JJ: Cardiac arrhythmias. *In* Wyngaarden JB, Smith LH (eds): Cecil Textbook of Medicine, ed 12. Philadelphia, Saunders, 1982, p 264; with permission.)

(2) recirculation of the impulse to its point of origin; (3) elimination of the arrhythmia by interrupting the pathway. These criteria are seldom fulfilled in clinical practice.

The pre-excitation syndromes are classic examples of situations in which re-entrant tachyarrhythmias occur. In the Wolff-Parkinson-White syndrome, myocardial strands provide an accessory electrical connection between the atria and ventricles.[4, 5] The accessory pathway usually exhibits faster conduction but greater refractoriness than the normal AV node pathway. If a premature atrial contraction occurs when the accessory pathway is refractory but the AV node is not, the impulse may be conducted in an anterograde fashion via the AV node to the ventricles and then retrograde via the accessory pathway to the atria. If this pattern is sustained, a tachycardia occurs. The QRS complex appears normal because the ventricles are excited via the AV node. In patients with Wolff-Parkinson-White syndrome, surgical interruption of the re-entry loop eliminates the arrhythmias.[41]

Myocardial ischemia and infarction may lead to marked inhomogeneity of refractoriness and conduction in adjacent ischemic and nonischemic ventricular myocardium. This facilitates re-entry processes that are probably responsible for many ventricular arrhythmias, although Mines' criteria are seldom fulfilled. Multiple wavelets of re-entry are likely responsible for flutter and fibrillation in the atria and the ventricles.[58]

Triggered Activity

Triggered activity can only be initiated in response to incoming electrical stimuli, and by definition, is not a form of abnormal automaticity. Excitation of affected myocardium results in a second peak or "after-depolarization" in the AP. This after-depolarization may initiate a premature beat if it occurs at a time when the surrounding myocardium is not refractory. After-depolarizations may arise early (phase 2 or 3) or late (phase 4) in the AP. They are due to abnormal ionic currents associated with high catecholamine levels, hypoxia, digitalis, and antiarrhythmic drugs. The importance of triggered activity in the pathogenesis of clinical arrhythmias is unclear.[43]

Invasive Electrophysiologic Testing

Intravascular recording and stimulating catheters can be introduced into the heart, permitting assessment of SA node function, evaluation of AV node conduction, and diagnosis of arrhythmias.[24, 26] Invasive electrophysiologic testing is useful in evaluation of conduction disorders, refractory malignant arrhythmias, and unexplained syncope. However, as the tests are associated with significant risk, indications and alternatives must be weighed carefully.

The His bundle electrogram is an intracardiac recording of voltage changes associated with sequential depolarization of the atria, His bundle, and ventricles. Using the His bundle electrogram, AV conduction can be divided into several components. By this means, conduction delay originating in the AV node can be distinguished from that occurring in the His Purkinje system. This has clinical importance, since infranodal block is more likely to be associated with serious bradyarrhythmias than AV nodal block.

Numerous techniques are used in the electrophysiologic evaluation of arrhythmias. Timed premature stimuli can induce and terminate arrhythmias and elucidate the mechanisms by which arrhythmias are initiated. Pacing may initiate or terminate arrhythmias and allow evaluation of anterograde and retrograde AV conduction and refractoriness. Electrophysiologic testing may differentiate between automatic and re-entrant arrhythmias. Re-entrant arrhythmias generally can be initiated by single or multiple extra stimuli administered during sinus rhythm or rapid pacing, whereas automatic arrhythmias cannot. In re-entrant arrhythmias there is also usually evidence of marked regional conduction delay.

THE ELECTROCARDIOGRAM

The ECG is a continuous record of voltage changes that reflect cyclic electrophysiologic events in the myocardium.[10, 15] It is usually recorded from the skin (the surface ECG), using electrodes that are connected to a galvanometer (the electrocardiograph). It can also be recorded from electrodes positioned in the esophagus, in the chambers of the heart, or directly on the myocardium.

With each heartbeat, the ECG inscribes a series of deflections that are labelled P, Q, R, S, T, and U (Fig. 4). The P wave reflects atrial depolarization while the Q, R, and S waves (the QRS complex) reflect ventricular depolarization. If the initial deflection of the QRS complex is negative, it is a Q wave. A positive deflection in the QRS complex is an R wave. A negative deflection succeeding an R wave is an S wave. The T wave corresponds to ventricular repolarization. The U wave is of indeterminate origin. The PR interval, from the onset of the P wave to the onset of the QRS complex, reflects the time required for conduction of the cardiac impulse from the SA node to the ventricles. The QT interval, from the onset of the QRS complex to the end of the T wave, indicates the time required for both ventricular depolarization and repolarization. The ST segment represents the period when the ventricles are completely depolarized, whereas the TP segment corresponds to the period when the heart is completely repolarized. The ECG is usually recorded as a plot of voltage versus time using a calibration of 10 mm per mV and a paper speed of 25 mm per second.

To understand the origin of ECG deflections one must be familiar with the concept of an electrical dipole. Positive and negative charges separated by a short distance constitute a dipole. The voltage or potential difference across the dipole can be represented by a vector, indicating its magnitude and orientation. By convention, the vector points from negative to positive. The electrical activity of the heart produces multiple depolarization and repolarization dipoles, which

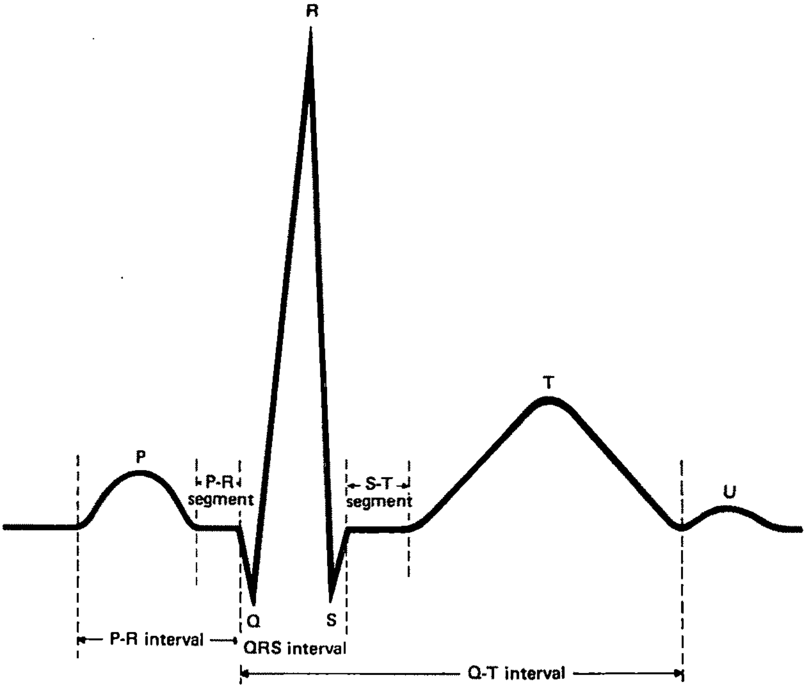


Figure 4. Waves and intervals of the electrocardiogram. (*From* Chung EK: Principles of Cardiac Arrhythmias, ed 3. Baltimore, Williams & Wilkins, 1983; with permission.)

may be summated as a single dipole vector. To model the ECG, we assume that the heart can be represented by a single dipole located at the center of a thorax, which has homogeneous conduction characteristics. The cardiac dipole generates an electric field that radiates from the center of the thorax. Using this model, the electrical potential that exists at any point on the surface of the thorax can be predicted from mathematical and physical principles.[44, 45]

To understand the origin of the ECG complex associated with the cycle of ventricular depolarization and repolarization, it is helpful to start by considering the voltage changes that would be recorded by electrodes positioned in proximity to a transmural strip of myocardium (Fig. 5). During the resting phase, the unstimulated strip is uniformly polarized (that is, positive on the outside of the cells). Therefore, there is no dipole or electrical field. The electrodes record no electrical potential and an isoelectric line is inscribed by the ECG. Stimulation of the strip at its endocardial side initiates depolarization, and a wave of surface negativity proceeds from endocardium to epicardium. The strip now becomes a dipole and generates an electric field that is detected by the electrodes. An electrode on the negative side of the dipole (that is, the endocardium) records a negative deflection, while

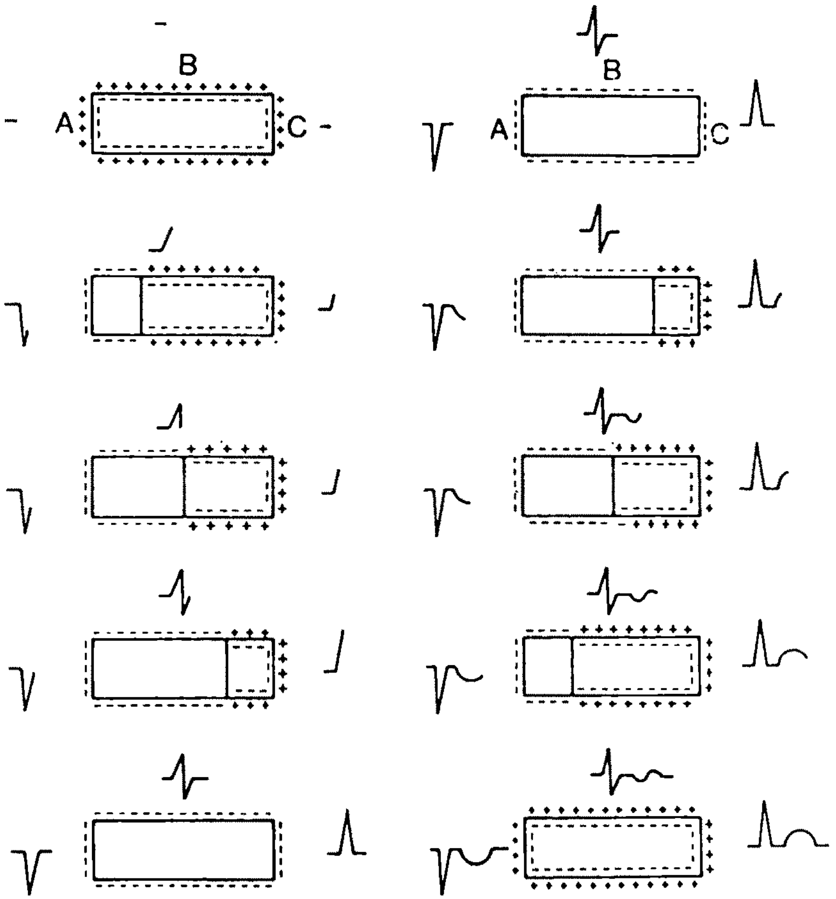


Figure 5. Potentials generated during depolarization (left vertical sequence of panels) and repolarization (right vertical sequence of panels) recorded with exploring electrodes located at the endocardium (*A*), epicardium (*C*), and midway between the two (*B*). (*Modified from* Barker JM: The Unipolar Electrocardiogram: A Clinical Interpretation. New York, Appleton-Century-Crofts, 1952; with permission.)

an electrode on the epicardial side records a positive deflection. An electrode in the middle of the strip records a biphasic deflection. When the wave of negativity reaches the epicardium, the strip is uniformly depolarized and the electrodes again record isoelectricity. The wave recorded during depolarization corresponds to the QRS complex of the normal ECG. In the intact heart, ventricular repolarization proceeds from epicardium to endocardium, so the polarity of the myocardial dipole is the same during both repolarization and depolarization. Thus, the ECG wave inscribed during repolarization, corresponding to the T wave of the ECG, is in the same direction as the R wave seen during depolarization. Dispersion in the rate of re-

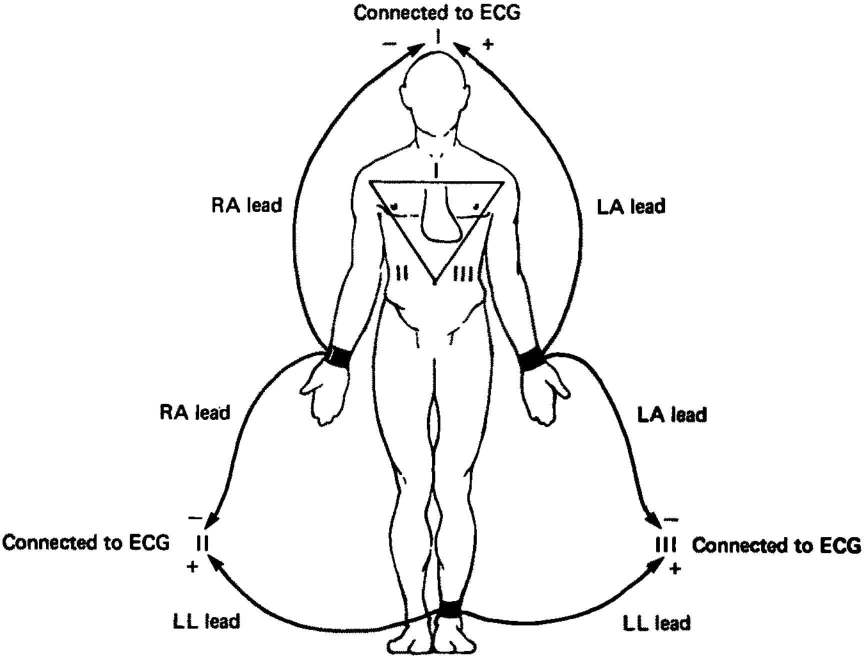


Figure 6. The connections for the bipolar standard leads (I, II, III) and Einthoven's triangle. (*From* Goldman MJ: Principles of Clinical Electrocardiography, ed 12. Copyright, Lange Medical Publications, 1986; with permission.)

polarization in various portions of the ventricles accounts for the relatively broad shape of the T wave compared with the narrow QRS complex.

Surface ECG leads reflect the projection of the cardiac dipole vector onto a particular lead axis. The lead axis is represented by a line joining two ECG electrodes, a positive or exploring electrode and a negative or indifferent electrode. Conventional ECG lead axes lie in either the frontal plane (the limb leads) or the transverse place (the precordial leads).

The limb leads are recorded from electrodes located on the right arm (RA), left arm (LA), and left leg (LL). The bipolar limb leads, I, II, and III, record the difference in potential between RA and LA, RA and LL, and LA and LL, respectively, with the latter electrode being positive in each case (Fig. 6). To record the so-called unipolar limb leads, all three extremity leads are connected to a central terminal. The central terminal serves as the indifferent electrode during the recording of unipolar leads. The central terminal is assumed to record zero potential, and to lie at the center of an equilateral (Einthoven's) triangle formed by the RA, LA, and LL electrodes. The unipolar leads record the difference in potential between one of the limb electrodes and the central terminal. The potential difference recorded by uni-

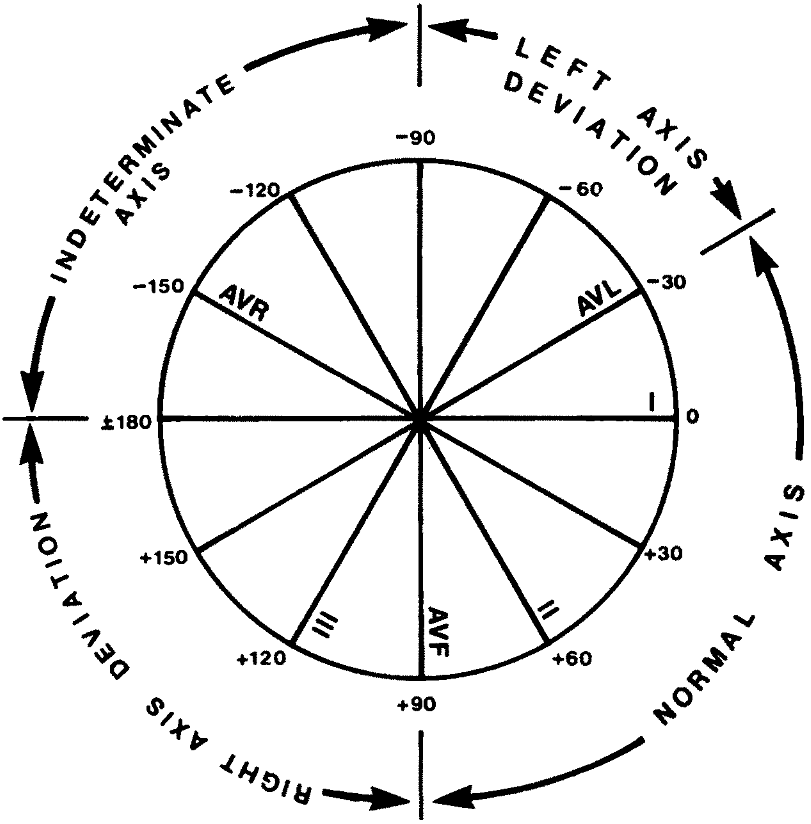


Figure 7. The frontal plane hexaxial reference system, indicating the 0 degree reference, the axes of the six limb leads (I, II, III, AVR, AVL, AVF) and the ranges of normal and abnormal frontal plane QRS axes of the heart. (*From* Fisch C: Electrocardiography and vectorcardiography. *In* Braunwald E (ed): Heart Disease: A Textbook of Cardiovascular Medicine, ed 3. Philadelphia, Saunders, 1988, p 186; with permission.)

polar limb leads is routinely augmented by disconnecting the extremity lead being recorded from the central terminal. The letter "V" designates a unipolar lead, and the prefix "a" indicates augmentation. Thus, the augmented unipolar limb leads are called aVR, aVL, and aVF. The six limb lead axes are represented on a hexaxial reference system in the frontal plane, with the lead I vector pointing from right to left and designated 0° (Fig. 7).

Precordial unipolar leads are recorded in a similar fashion, but are not augmented. They record the potential difference between electrodes on the chest wall and the central terminal (Fig. 8), and are designated as leads V1 to V6. Generally, leads V1 and V2 face the right side of the ventricular septum, leads V3 and V4 the septum itself, and leads V5 and V6 the left side of the septum.

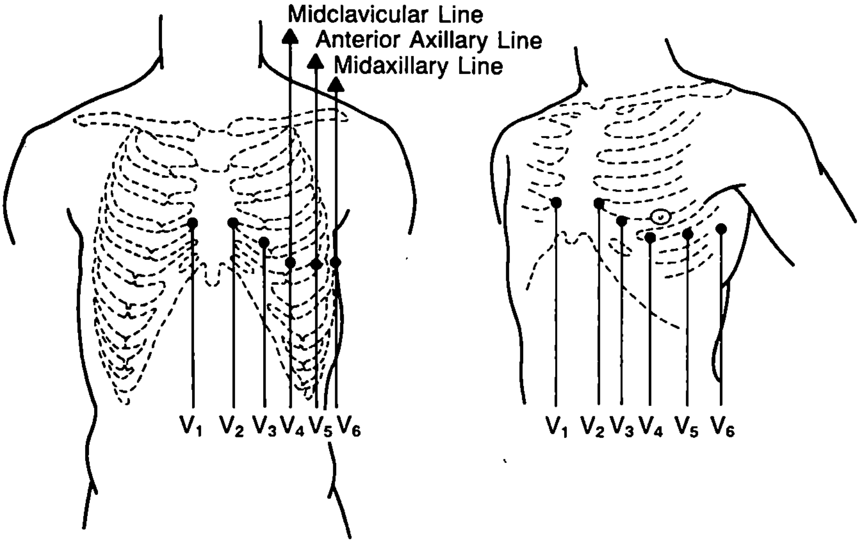


Figure 8. The positions of the unipolar precordial leads (V1 to V6). (*From* Atlee JL: Perioperative Cardiac Dysrhythmias: Mechanisms, Recognition, Management. Chicago, Year Book Medical, 1985, p 103; with permission.)

The Normal Electrocardiogram

The wave of atrial depolarization begins at the SA node and proceeds leftward, inferiorly, and posteriorly. The resulting surface ECG potential, the P wave, is rounded and is normally less than 0.20 mV in amplitude and 0.12 seconds in duration. The P wave is positive in all precordial leads except for V1 where it may be biphasic or negative. Atrial repolarization is recorded as the Ta wave, which is opposite in polarity to the P wave. Because atrial repolarization normally occurs simultaneously with ventricular depolarization, the Ta wave is usually obscured by the QRS complex. The PR interval represents intra-atrial, AV nodal, and His Purkinje conduction, and its duration varies from 0.12 to 0.20 seconds.

The QRS complex of ventricular depolarization can be described by four sequential vectors (Fig. 9): (1) initial septal activation from left to right and anteriorly; (2) a wave of excitation involving both ventricles, directed inferiorly and slightly to the left; (3) unopposed activation of the apical and central portions of the left ventricle after completed right ventricular depolarization, with the vector directed posteriorly, inferiorly, and to the left; and (4) activation of the posterior basal portion of the left ventricle and septum, with the vector directed superiorly and posteriorly.[15] As ventricular activation occurs quite symmetrically about the septum, much of the voltage is cancelled by opposing forces.

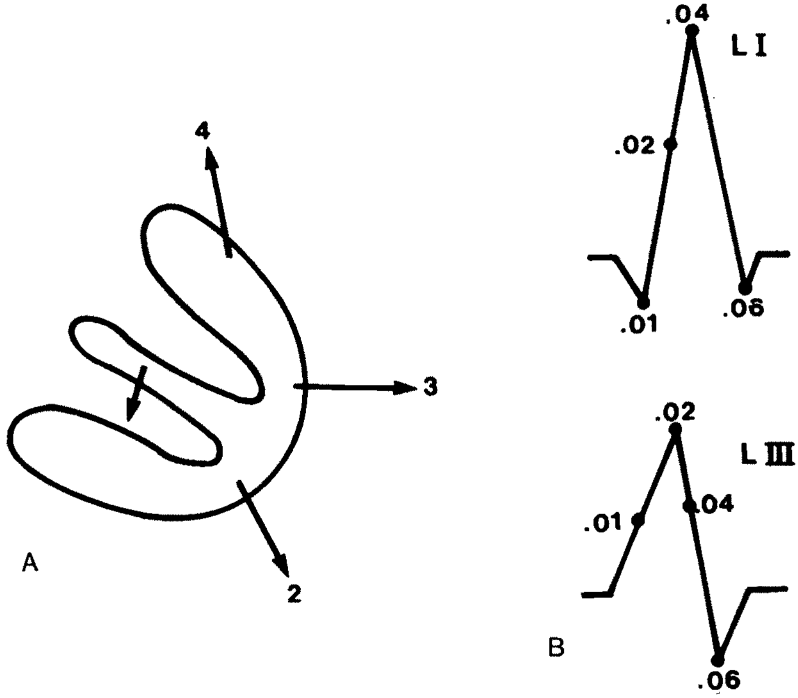


Figure 9. Correlation between the order of ventricular activation (*A*) and the QRS complex of the ECG in leads I and III (*B*). (*A*) The order of ventricular activation is represented by four sequential frontal plane vectors. (*B*) The QRS pattern inscribed by the four vectors and the corresponding times in seconds. (*Modified from* Fisch C: Electrocardiography and vectorcardiography. *In* Braunwald E (ed): Heart Disease: A Textbook of Cardiovascular Medicine, ed 3. Philadelphia, Saunders, 1988, p 185; with permission.)

Septal activation (vector 1) results in a Q wave in left-sided leads I, II, aVL, V5, and V6, and an initial R wave in the right precordial and septal leads V1 to V4. Vector 2 inscribes an R wave in leads II, III, V3, and V4. Vector 3 produces an R wave in the standard limb leads, aVL, aVF, V5, and V6, with an S wave in leads aVR and V1 through V3 or V4. Vector 4 may produce a terminal S wave in leads I, V5, and V6. Normal duration of the QRS complex is 0.12 seconds or less.

Cardiac chamber enlargement and bundle branch block produce ECG changes that are predictable from their effects on the vectors of depolarization and repolarization.[15] For example, in LBB block, septal depolarization proceeds from right to left and the normal Q waves are no longer apparent in left-sided ECG leads. Left ventricular depolarization is slowed and QRS duration is increased. Delay in left ventricular repolarization produces secondary ST-segment depression and T-wave inversion in left-sided leads.

QRS Axis and Rotation

The electrical axis of the heart is the direction of the vectorial sum of all the instantaneous vectors of ventricular depolarization. Usually, only the projection of this vector in the frontal plane is considered. An accurate frontal QRS axis determination accounts for both the magnitude and duration of QRS voltage. Clinically, however, frontal QRS axis is determined by summing the vectors of QRS voltages (that is, R wave voltage minus Q and S wave voltage) in a pair of perpendicular limb leads (for example, I and aVF). The frontal QRS axis can also be approximated by noting that it is nearly parallel to the limb lead with the largest net positive or negative QRS deflection, and nearly perpendicular to the lead with the smallest deflection. For example, a maximum positive QRS magnitude in lead aVL and minimum QRS in lead II occurs with axis of −30 degrees (see Fig. 7). An axis of −30 to +90 degrees is normal, −30 to −90 degrees is left axis deviation, +90 to +180 degrees is right axis deviation, and −90 to −180 degrees is indeterminate. Left axis deviation occurs normally, but also with left ventricular hypertrophy, LBB block and left anterior divisional block. Right axis deviation may be normal, but also occurs with right ventricular hypertrophy, RBB block, and left posterior divisional block.

The QRS orientation in the transverse plane is estimated by inspecting the QRS complex in the precordial leads. This is described as it would appear to an observer on the diaphragmatic side. The transition zone, the point where QRS morphology switches from a dominant S wave (that is, S wave larger than R wave) to a dominant R wave, is usually between leads V3 and V4. In clockwise rotation, the transition zone shifts to the patient's left and the precordial leads reflect predominantly right ventricular and septal activity. With counterclockwise rotation, the transition zone shifts to the patient's right and the precordial leads reflect predominantly left ventricular activity. The transition zone may be shifted because of myocardial infarction, ventricular hypertrophy, or normal anatomic variation in cardiac position.

ST Segment, T Wave, and U Wave

The ST segment is normally isoelectric, but ST-segment elevation (usually < 0.2 mV) is often noted in precordial leads in normal patients.[21] The most important cause of a pathologically elevated or depressed ST segment is myocardial ischemia. This will be discussed in detail later. In adults the T wave is upright except in leads aVR and occasionally V1. Abnormalities of the T wave characterize many pathologic situations, the most common of which is ischemia.

The U wave may reflect Purkinje fiber repolarization or a mechanical event like ventricular relaxation. Normally it is an upright rounded wave with amplitude 5 to 50 per cent that of the T wave. It is often not visible. Pathologic positive U waves accompany hypokalemia and negative U waves are a marker of severe coronary disease.

The QT Interval

An increased QT interval reflects prolongation of ventricular depolarization and repolarization. The most common causes are acquired myocardial disease, electrolyte disturbances, drug effects, and congenital long QT-interval syndromes.[15] Prolongation of the QT interval may be associated with serious arrhythmias, including torsades de pointes, a form of ventricular tachycardia. As QT interval varies with heart rate, it is often corrected using Bazett's formula: $QTc = QT/\sqrt{RR}$ interval, where RR interval is the period in seconds between successive R waves.[3] Upper limits of normal for QTc are 0.39 seconds in men and 0.44 seconds in women.

ISCHEMIA AND INFARCTION

Myocardial ischemia and infarction have major effects on the cellular AP, and cause ST-segment and T-wave abnormalities and pathologic Q waves. Ischemia may cause both partial depolarization during phase 4 (that is, a less negative RMP), and decreased magnitude of the plateau of phase 2 (that is, a less positive plateau), or "early repolarization."[29, 53] Ischemia may delay depolarization or repolarization and alter AP duration.[29, 52] The ECG changes of ischemia are a consequence of these alterations in cellular electrophysiology in ischemic myocardium. What follows is a rationalization of the ST-segment and T-wave changes accompanying ischemia. Explanations of ST-segment changes are well grounded in experimental work, while the T-wave effects, which are clinically less consistent, remain an area of active research.[51]

ST-Segment Depression

Normally, during diastole, the ventricles are uniformly polarized. Therefore, no cardiac dipole exists and the corresponding TP segment of the ECG is isoelectric. However, because of membrane dysfunction, cells in an area of subendocardial ischemia are slightly depolarized at this time (Fig. 10). Thus, the surface of ischemic cells is negatively charged relative to adjacent normal cells. A precordial or epicardial electrode would record a positive potential, which would be inscribed as TP-segment elevation on the ECG. The degree of TP-segment elevation is measured with respect to the ST segment. By convention this TP-segment displacement is described as ST-segment depression rather than TP-segment elevation. The magnitude of the AP in ischemic subendocardial cells may also be decreased. Therefore, during phase 2 of the AP in systole, ischemic cells are less depolarized, and their surfaces are positively charged relative to normal cells. A precordial or epicardial electrode would record this negative potential as electrocardiographic ST-segment depression. Thus, dur-

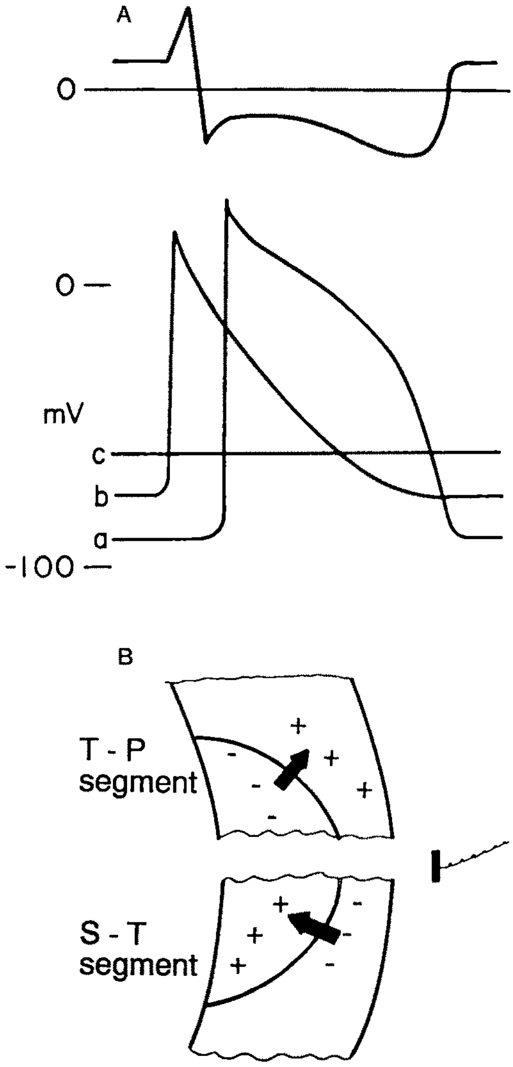


Figure 10. Abnormal depolarization and repolarization in subendocardial ischemia. (*A*) The upper trace is a surface electrocardiogram with an isoelectric reference line, recorded overlying an area of subendocardial ischemia. The lower traces are three intracellular action potential (AP) recordings from (*A*) a normal epicardial cell, (*B*) an ischemic subendocardial cell with a partially depolarized (less negative) resting membrane potential and an abbreviated (less positive) AP, (*c*) an ischemic subendocardial cell depolarized enough to render it inexcitable. (*B*) During the resting phase (TP segment, upper diagram) the surface of partially depolarized ischemic subendocardial cells is negatively charged relative to epicardial cells. The resultant vector directed toward the epicardial surface produces TP-segment elevation on the ECG. During the plateau phase of the AP (ST segment, lower diagram) the surface of ischemic subendocardial cells is positive relative to epicardial cells. The resultant vector directed toward the endocardium produces ST-segment depression on the ECG. As all changes on the ECG are referenced to the ST segment, both processes are interpreted as ST-segment depression. (*Modified from* Fozzard HA, DasGupta DS: ST-segment potentials and mapping: Theory and experiments. Circulation 54:533, 1976; by permission of the American Heart Association.)

ing subendocardial ischemia, both diastolic and systolic injury potentials contribute to ST-segment depression in surface ECG leads.

ST-Segment Elevation

The same concepts explain the ECG changes of subepicardial ischemia. A precordial or epicardial electrode adjacent to an area of subepicardial ischemia would record a negative potential during diastole (TP segment), which would be inscribed as an ST-segment elevation on the ECG. This electrode would also record a positive potential during systole, a "true" ST-segment elevation. Transmural ischemic processes produce ECG patterns similar to those of subepicardial ischemia. Pericarditis also causes ST-segment elevation, which is usually concave upward, unlike that in ischemia, which tends to be convex upward.

T-Wave Changes

Ventricular repolarization normally proceeds from epicardium to endocardium, in the opposite direction from depolarization. For this reason the T wave is normally upright in precordial ECG leads. With subendocardial ischemia, the normally later subendocardial repolarization may be further delayed, thus increasing and prolonging the potential difference between subepicardium and subendocardium. This increases T-wave amplitude in precordial epicardial leads (Fig. 11*B*). When ischemia is subepicardial, repolarization of this area will be delayed and the normal order of repolarization will be reversed, resulting in inverted T waves in epicardial leads (Fig. 11*C*).

Myocardial Infarction and Q Waves

The ECG diagnosis of myocardial infarction is best established by the observation of serial changes, although up to a third of patients do not manifest the classical pattern.[1] Serial changes differentiate between infarction and other conditions associated with ST-segment elevation such as pericarditis, hyperkalemia, ventricular aneurysm, coronary spasm, and normal early repolarization.[15] The sequence begins with T-wave changes including prolongation, increased amplitude, or inversion. This is followed by ST-segment elevation in ECG leads oriented over the epicardial surface of the infarcted area. As the ST-segment elevation resolves, Q waves and T-wave inversion develop. Infarcted muscle is electrically inactive and does not contribute to the vector of depolarization, which therefore must be directed away from the infarction.[11] Thus, pathologic Q waves are inscribed in leads facing the infarction. The ECG diagnosis of completed myocardial infarction depends on the presence of pathologic Q waves exceeding 0.03 seconds in duration.

The leads in which Q waves appear correlate quite well with infarction location.[7] Occlusion of the RCA usually causes inferior myocardial infarction with serial ECG changes in inferior leads II, III and aVF. Left anterior descending artery occlusion typically causes anteroseptal infarction and ECG changes in leads V1 to V4, whereas CCA occlusion causes anterolateral infarction and ECG changes in leads I, aVL, V5, and V6.

Pathologic Q waves may be absent in transmural and present in nontransmural infarction. Therefore, these terms should be avoided in the description of ECG findings. In the absence of infarction, Q waves occur after cardiac surgery and in myocardial disease including myocarditis, amyloidosis, neuromuscular disorders, and hypertrophic cardiomyopathy.

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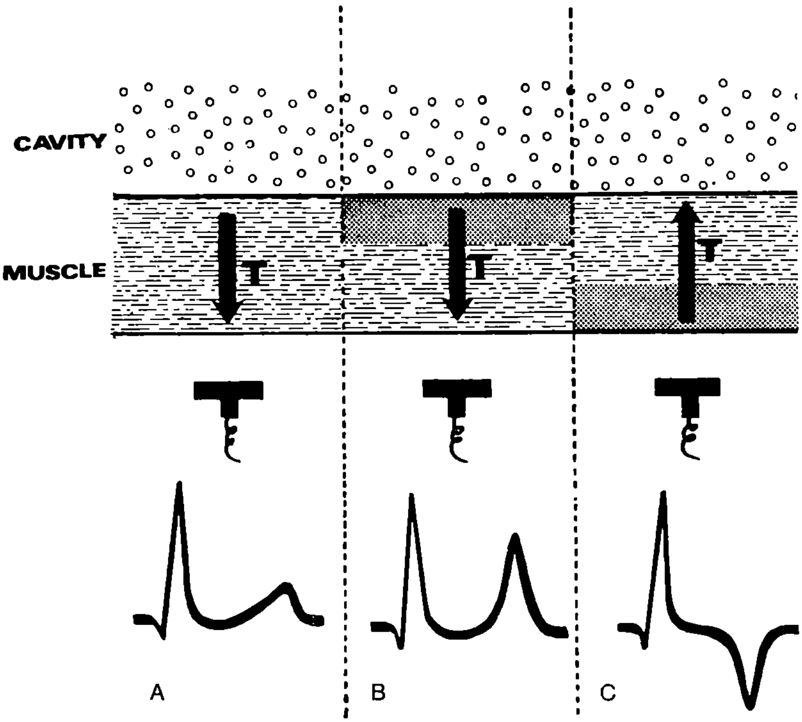

Figure 11. The T wave in ischemia. (*A*) Normal repolarization proceeds from epicardium to endocardium. The T-wave vector is directed from endocardium to epicardium, and the T wave is upright in epicardial ECG leads. (*B*) Subendocardial ischemia (*dotted area*). The normally later subendocardial repolarization is further delayed, exaggerating the potential difference between subendocardium and subepicardium. Thus, the T wave increases in amplitude. (*C*) Subepicardial ischemia (*dotted area*). Subepicardial repolarization is delayed and the order of repolarization is reversed. The T-wave vector is directed from epicardium to endocardium and the T wave is inverted. (*Modified from* Schamroth L: The Electrocardiology of Coronary Artery Disease, ed 2. Oxford, Blackwell Scientific Publications, 1984, p 7; with permission.)

ELECTROCARDIOGRAPHIC LEAD SYSTEMS: PERIANESTHETIC USE

Lead Configurations

Conventional ECG systems for perioperative use employ three, four, or five electrodes. The five-electrode system is best for both rhythm analysis and detection of ischemia, although three-electrode systems are often adequate.

Table 2. *Bipolar Leads for Use with Three Electrodes**

BIPOLAR LEAD	NEGATIVE ELECTRODE	POSITIVE ELECTRODE
II	Under right clavicle	Left leg
MCL1	Under left clavicle	V1
CS5	Under right clavicle	V5
CM5	Manubrium	V5
CB5	Center of right scapula	V5
CC5	Right anterior axillary line (V5R)	V5

* The third electrode is a ground. Its position is important only when there is capability to monitor more than one lead.

The five-electrode system includes electrodes located on each extremity plus one in a precordial position (usually V5). The right leg electrode serves as a ground. With this system the six limb leads and V5 can be recorded.

Systems employing three electrodes (negative, positive, and ground) record up to three bipolar leads. By changing electrode positions, a variety of bipolar leads may be recorded (Table 2). When referring to bipolar leads other than I, II, and III, the letter "C" indicates central placement of the negative electrode. The prefix "M" indicates a lead position is modified. The suffix "L" or "R" denotes body side, and a number suffix indicates precordial lead position. For example, lead MCL1 has its negative electrode in a left subclavian position (modified from the left arm), and its positive electrode in a V1 position. A letter suffix may also indicate anatomic electrode location (for example, CS5 for subclavian). When a three-electrode system is used in patients with coronary artery disease, we recommend that electrodes be placed under the right clavicle, in the V5 position, and on the left leg. This allows monitoring of both leads II and CS5.

Rhythm Monitoring

For accurate rhythm analysis, one must be able to identify and differentiate between atrial and ventricular ECG activity. Leads V1, MCL1, and CB5 are sensitive leads for rhythm analysis, with both prominent P waves and QRS complexes. Lead II records prominent P waves but the QRS complex may not be optimum for rhythm analysis.

Unipolar and bipolar esophageal leads are also very useful. Kates et al,[30] using leads II and V5, were able to correctly diagnose intraoperative arrhythmias in 54 and 42 per cent of cases, respectively. Using an esophageal lead, they made the correct diagnosis in all. Intracardiac leads are also useful for diagnosis of arrhythmias. Formerly, saline-filled catheters were used, but nowadays Swan-Ganz catheters with pacing electrodes can be used for perioperative intracardiac recording.[38, 57] Arrhythmia analysis is easier when serial paper recordings are available for comparison.

Ischemia Monitoring

The ECG is less sensitive than transesophageal echocardiography for the detection of myocardial ischemia.[12, 49] Nonetheless, the ECG remains the simplest, least invasive, and least expensive technology for diagnosing ischemia, and it is universally available. Therefore, it is an extremely important tool for monitoring and treating patients with coronary artery disease.

Filters used in ECG processing have both beneficial and detrimental effects on tracing quality. Some machines have a "monitor" mode that filters out frequencies below 4 Hz. This reduces baseline variation caused by respiration and other patient movement. However, this mode may cause significant ST-segment distortion and should not be used for the diagnosis of ischemia. The "diagnostic" ECG mode, which incorporates only a 0.1 Hz filter, avoids the problem of inaccurate ST-segment reproduction, but may introduce baseline variability.[2, 40]

The criteria for the electrocardiographic diagnosis of myocardial ischemia are controversial. Generally, ST-segment displacement is quantitated 60 or 80 msec after the J point. The J point corresponds to the change in slope that initiates the transition from S wave to ST segment. The degree of ST displacement is measured with respect to either the PR or TP segment. On electrophysiologic grounds ST-segment displacement should be measured with respect to the TP segment. In practice, however, the PR segment is more consistently identifiable. The degree of ST displacement is quantitated in millivolts. The standard ECG calibration is 0.1 mV per mm. A diagnosis of subendocardial ischemia requires ≥ 0.1 mV (that is, 1.0 mm) of new, horizontal, or downsloping ST depression, or ≥ 0.15 mV if the ST segment is upsloping. The diagnosis of transmural myocardial ischemia requires 0.15 mV ST-segment elevation. The specificity of these diagnoses will be greatly increased when ST-segment displacement persists for ≥ 1 minute.

Precordial leads are superior to limb leads for the detection of ischemic ST-segment changes.[6] Precordial lead V5 is most sensitive, detecting 89 per cent of significant ST-segment depressions during exercise. Sensitivity is increased to 94 per cent when precordial leads V3, V4, and V6 are added to V5, and to 100 per cent when data from inferior leads II and aVF are included. Recently, London et al[37] obtained continuous 12-lead ECG recordings during general anesthesia in 105 patients with documented or suspected coronary artery disease. They found leads V5 (75 per cent) and V4 (61 per cent) were most sensitive for detection of ischemia. Leads II, V3, and V6 (33, 24, and 37 per cent, respectively) were less sensitive. These studies demonstrate the pre-eminent importance of precordial leads in intraoperative detection of ischemia. They also indicate that the combination of leads V5 and II sacrifices some sensitivity to ischemia for improved rhythm analysis. The large difference in sensitivity between leads V5 and V6 emphasizes the critical importance of precise electrode placement. Bipolar modifications of V5 including CS5, CM5, and CB5 are also sensitive to ischemic ST-segment changes.[22] An electrode in the V4 position on the right side (V4R) is sensitive for right ventricular ischemia and infarction and should be recorded in patients suspected of having these problems.[32]

Myocardial ischemia implies an imbalance in myocardial oxygenation. Until recently, ischemia was thought to be a consequence of changes in systemic hemodynamics that either increased oxygen demand or decreased supply. However, recent studies employing ambulatory electrocardiographic monitoring indicate that, in patients with coronary disease, ischemic episodes are more frequent than anginal symptoms would indicate.[13, 46] Many ischemic episodes are silent and are not associated with abnormal systemic hemodynamics. These observations suggest that decreases in myocardial oxygen supply caused by alterations in coronary vascular tone are an important cause of myocardial ischemia. Studies employing perioperative ECG monitoring confirm that ischemic ST-segment changes in high-risk surgical patients are frequently unaccompanied by angina or major changes in heart rate or blood pressure.[33, 48] Therefore, anesthesiologists must search vigilantly for ischemic ECG changes even when hemodynamics are normal or symptoms are absent. Unfortunately, experienced clinicians, with a high index of suspicion will fail to detect the majority of transient intraoperative ST-segment changes.[37] Computerized ST-segment trending may provide a solution to these problems.[34]

ST-Segment Trend Monitoring

The anesthesiologist's ability to recognize and treat significant intraoperative ST-segment abnormalities can probably be enhanced by continuous computerized ST-segment analysis with simultaneous digital and trend display.[34] In one such system (Marquette Electronics Inc, Milwaukee, WI) a baseline ST-segment template is established for each of three ECG leads. The isoelectric reference point, and the point at which the ST segment is quantitated are displayed and can be manually adjusted. The templates are continuously updated and replaced by new matching complexes. The system continuously displays a trend, updated every 15 seconds, representing the sum of the absolute values of ST-segment displacements in the three monitored leads. A positive trend alerts the clinician to the possible development of myocardial ischemia.

Continuous ECG monitoring and ST-segment analysis in ambulatory subjects is a powerful research tool that promises to revolutionize our understanding of perioperative myocardial ischemia.[33] The QMed monitor (QMed Inc, Clark, NJ) is a light, compact, solid-state FM ambulatory monitor that exemplifies the rapid advance of technology in this area.[2a, 36a] The input from a single ECG lead is filtered, amplified, and then converted from an analog to a digital signal. It is then analyzed by a microprocessor according to an algorithm stored in the unit. Computerized analysis of the ST segment involves recognition of the QRS complex and subsequent definition and measurement of ST-segment depression. Data regarding significant ST-segment depression are stored in the random-access memory of the unit. The unit can be programmed to recognize a certain degree and duration of ST-segment depression as significant. The minimum, maximum, and median heart rate from 15-minute intervals, the number and duration of ischemic events, an ST-segment histogram, and "sample strips" of ST-segment depression, are transmitted through an optical interface at the end of the recording period and printed as hard copy.

SUMMARY

The cardiac electrical impulse is rhythmically initiated in the SA node and sequentially conducted to the ventricular myocardium by the specialized conducting system. Resting membrane potential is determined by the distribution of ions across the selectively permeable cardiac cell membrane. The AP is a sequence of membrane permeability and transmembrane potential changes accompanied by transmembrane ion currents. Arrhythmias occur due to abnormalities of cellular electrophysiology that affect automatic activation or impulse conduction by cardiac cells. The ECG is a continuous recording of body surface voltage changes accompanying the cardiac electrical impulse. Cellular electrophysiologic and vectorial principles are used to help us conceptualize the normal ECG and the changes that occur with myocardial ischemia and infarction. Electrocardiographic lead systems for perioperative use are chosen in order to maximize the anesthesiologist's ability to assess cardiac rhythm and detect myocardial ischemia. Computerized ambulatory ECG monitoring and ST-segment trending are expanding our understanding of perioperative ischemic events.

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Diagnosis and Management of Intraoperative Arrhythmias

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The Etiology of Intraoperative Arrhythmias

Scott R. Springman, MD, and John L. Atlee, MD†*

Among the most common vexing and perplexing problems encountered in the operating suite is the patient with an abnormal cardiac rhythm. It is said that some type of arrhythmia occurs during the perioperative period in at least 60 per cent of patients.[23] The prevalence of rhythm abnormalities, of course, depends on the method one uses to document their existence. Continuous Holter recording will disclose many more than the usual technique of periodically watching an electrocardiogram (ECG) monitor. Certainly, one must first perceive the existence of a rhythm disorder before a diagnosis and subsequent corrective measures are taken. In the operating suite, we interpret the implications of arrhythmias differently depending on the type, acuteness and duration, clinical setting, the patients' general condition, and, finally, the hemodynamic consequences. However, the abrupt onset of an arrhythmia should be regarded a sign of an underlying problem rather than as a final diagnosis. When feasible, the anesthesiologist should seek possible causes and aggravating factors before embarking on specific treatment. The causes for arrhythmias under anesthesia are many. Some are relatively innocuous, such as heightened vagal tone causing bradycardia in fit individuals. Some portend serious problems, such as hypoxemia from deteriorating lung function resulting in bradycardia. It is of paramount importance that intraoperative arrhythmias be viewed within this framework in order to make rational decisions about possible therapy.

This article reviews the electrophysiologic mechanisms for both normal and abnormal cardiac electrical activity. These mechanisms play an integral role in determining the type of arrhythmia generated. Also, commonly encountered clinical causes of these arrhythmias are discussed.

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CARDIAC ELECTROPHYSIOLOGY

An understanding of the ionic events responsible for the cardiac action potential (AP) will aid in the understanding of the cellular mechanisms for arrhythmias.[11] The concentration of ions inside and outside the cardiac cell are quite different. The origin of these cellular ion gradients can be traced to ATP-dependent $Na^+ \bullet K^+$ pumps in the cell membrane. These pumps keep the Na^+ concentration low and the K^+ concentration high inside the cells. Ions flow down these concentration gradients when specific membrane ion channels open in response to various stimuli. Potassium flowing out of the cell makes the membrane potential more negative (repolarization). Sodium or Ca^{++} flowing into the cell makes the membrane potential less negative (depolarization). If the K^+ flow decreases or Na^+ or Ca^{++} flow increases, the cell will depolarize at a variable rate, depending on the magnitude of these ion-flow changes. When the membrane potential reaches a certain value, called the threshold potential, a stereotypic depolarization and repolarization process, the AP, occurs. The generation of the AP is discussed for each of the fiber types.

The shape of the cardiac AP depends on the ionic mechanisms responsible for the component phases (Fig. 1). In general, there are cells that typically display spontaneous depolarization (pacemakers) and those that usually do not. During diastole, or phase 4, cells in the sinoatrial (SA) node, other latent atrial pacer sites, atrioventricular (AV) node, and ventricular Purkinje system normally show spontaneous depolarization. The Purkinje cells (Fig. 1*A*) are "fast response" types that have the following characteristics: (1) the maximum negative diastolic potential is about −80 to −90 mV; (2) the threshold potential is usually greater than 70 mV; (3) phase 0 is rapid; (4) there is an early, rapid phase 1 repolarization; and (5) the AP is completed by a phase 2 plateau, and a phase 3 final repolarization. In contrast, the SA and AV nodes (Fig. 1*B*) are "slow response" cells. They exhibit features as follows: (1) the maximum diastolic potential is about −40 to −70 mV; (2) the threshold potential is less than 70 mV; (3) phase 0 is slower; and (4) phase 1 is not apparent.

As opposed to pacemaker cells, the atrial and ventricular contractile cells (Fig. 1*C*) are usually all fast response fibers that exhibit AP characteristics similar to Purkinje cells, except that there is no spontaneous depolarization in phase 4. Instead, there is a flat "resting membrane potential" that remains between −80 and −90 mV until a depolarization and AP is generated by impulses originating from a pacemaker site.

Rapid inward flow of Na^+ cause the characteristic phase 0 rapid depolarization in fast response cells. The resting membrane potential has significant effects on this Na^+-dependent phase 0 because Na^+ channels are inactivated at less negative membrane potentials. When the resting membrane potential is more negative than −80 mV, all the Na^+ channels are available to open during an AP. When the resting

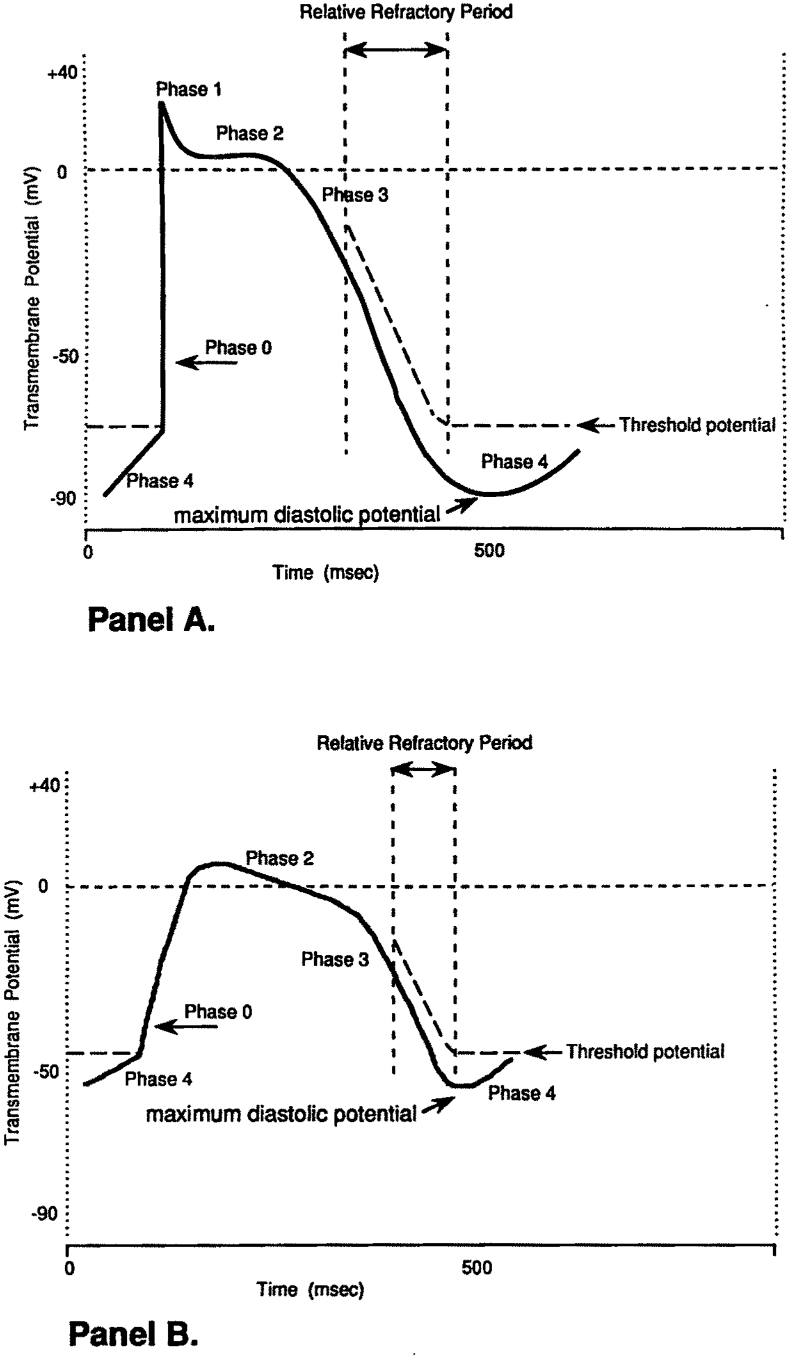
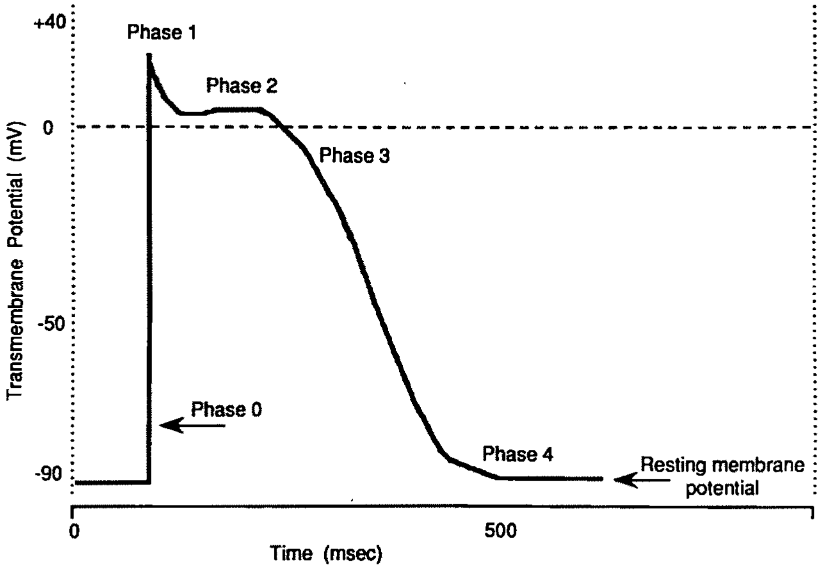


Figure 1. Stylized cardiac action potentials from fast and slow cells. (*A*) A typical action potential from a fast response fiber displaying automaticity (Purkinje). (*B*) Action potential from a slow response fiber displaying automaticity (SA and AV nodes).

Figure continued on following page.



Panel C.

Figure 1 (*Continued*). (*C*) A fast response action potential from cardiac muscle, not usually showing automaticity.

membrane potential is less negative, −70 to −60 mV, only half of Na^+ channels can open, whereas at about −50 mV, none can be opened. In fact, at resting membrane potential less negative than −50 mV, phase 0 of an AP is mainly generated by slow Ca^{++} rather than fast Na^+ current. Fast fiber APs, therefore, rely on Na^+ flow, whereas slow response fibers or "depressed" fast fibers (those whose diastolic potential is less negative than −50 mV owing to loss of membrane potential) rely on Ca^{++} flow. Further, Ca^{++} channels open and close more slowly than Na^+ channels. In addition, also unlike Na^+ flux, Ca^{++} ion flows can be increased by stimuli that raise intracellular levels of cyclic AMP. Loss of membrane potential from, for example, ischemia may lead to nonuniform conduction and favor re-entrant arrhythmias, as will be discussed later.

Completing the discussion of the AP is the repolarization process, which is fairly complex. Briefly, it appears that rapidly changing K^+ currents are primarily responsible. The repolarization process brings the cell back to its maximum diastolic potential or resting potential so that it is ready for another depolarization. At some point prior to resting potential, the cell may again be stimulated into generating an AP but the threshold potential is less negative (the "relative refractory period," see Fig. 1A).

These ionic mechanisms, as well as other factors, ultimately determine the special properties of the cardiac cell that are important in producing the electrical events leading to contraction. Three essential properties of cardiac fibers are (1) automaticity, (2) excitability, and (3) conduction.

Automaticity

Automaticity, or spontaneous diastolic (phase 4) depolarization, is characteristic of the cells in the SA node, which are normally the dominant pacemakers, and of other subsidiary or latent pacemaker cells found in the atria, the AV node and junction, and the His Purkinje system. Subsidiary pacemakers are normally suppressed by impulses originating in the SA node, and, usually, automaticity in these pacemakers occurs more slowly as one moves down from the SA node toward the ventricle.

Excitability

Another property that cardiac cells display is excitability, which indicates the ability of the cells to respond to stimuli with an AP. The smaller the difference between the resting membrane potential and the threshold potential, the more likely that an AP will result from any stimulus. Timing of a stimulus is also quite important; there is a period of time after an AP when a subsequent AP cannot be generated: the absolute refractory period. Following that is a time when a greater than usual stimulus is needed to produce an AP: the relative refractory period (see Fig. 1A). The presence of uniformity in cardiac refractory periods aids the orderly sequence of activation and conduction.

Conduction

Normally, the impulse initiated from the SA node spreads throughout the atrium, causing an atrial contraction. The impulse slows as it traverses the AV node (providing time for ventricular filling), then continues through the common His bundle before dividing into the right and left main bundle branches. The left bundle often further subdivides into the anterior and posterior bundle fascicles before they and the right bundle disperse into the Purkinje network, which activates the ventricular muscle mass. The heart uses this specialized conduction system to produce a coordinated contraction. As a general rule, fibers with more negative maximum diastolic potential (those that rely on fast Na^+ channels to produce phase 0) also conduct impulses rapidly, whereas those that use Ca^{++} channels for phase 0 conduct more slowly. In other words, the speed of conduction is largely a function of the maximum diastolic potential in the cell.

ELECTROPHYSIOLOGIC AND CELLULAR MECHANISMS OF ARRHYTHMIAS

Having reviewed the basic electrophysiology of normal cardiac function, we are ready to consider the etiologies of arrhythmias. These can be divided into three broad categories: (1) disorders of impulse generation (automaticity); (2) disorders of impulse propagation; and (3) disorders involving both impulse initiation and propagation.[14]

Abnormal Automaticity

Automaticity can be abnormal when certain cells, whose spontaneous phase-4 depolarization is ordinarily suppressed or reset by propagated APs from the SA node, reach threshold potential *before* the SA node fires. These cells can be those with normally Ca^{++}-dependent APs, or depressed fast response fibers (see following). Enhanced automaticity can produce one or more premature beats or can develop into a sustained tachycardia. Conditions that *reduce* the time it takes to reach threshold potential *increase* the rate of automaticity (Fig. 2). This can occur when the slope of phase-4 spontaneous depolarization is increased by catecholamine stimulation, when the threshold potential becomes more negative (for example, with decreased vagal activity), and when the maximum diastolic potential becomes less negative (for example, ischemia). Factors that reverse these processes will reduce the rate of automaticity. For example, the release of acetylcholine from increased vagal activity will increase the permeability of the cell membrane to K^+ ions. This loss of positive ions makes the maximum diastolic potential more negative and further from threshold potential. It also decreases the slope of phase-4 depolarization and makes the threshold potential less negative (that is, further away from the maximum diastolic potential).

Afterpotential and Triggered Arrhythmias

During late phase 3 or early phase 4 there can be spontaneous depolarizations, termed after-potentials, that can reach threshold potential and initiate APs.[7] An AP so initiated is called a "triggered" AP and is dependent on a previous depolarization for its production. If sustained rhythmic activity results from this process, the rhythm is a triggered rhythm. The full clinical implications of this are, as yet, uncertain, although after-potentials and triggering may be the mechanism for some digitalis- or ischemia-induced arrhythmias.

Abnormal Conduction

At any point in the conduction path from the atria to the ventricles, the propagation sequence can be accelerated, slowed, or totally blocked. Various abnormal anatomic pathways can bypass the normal sequence of activation and result in "ventricular pre-excitation." This may produce only shortened AV conduction or, in concert with other abnormalities such as atrial flutter/fibrillation, can produce dangerous ventricular rates during tachycardia. Accessory pathways can also be involved with re-entry, as we shall discuss. Recent reviews discuss the nomenclature and treatment of arrhythmias produced by these paths[46] and supraventricular tachycardia in general.[25] AV accessory pathways are the most common (Kent's bundle). Others include the James and Mahaim types. The AV accessory pathways are responsible

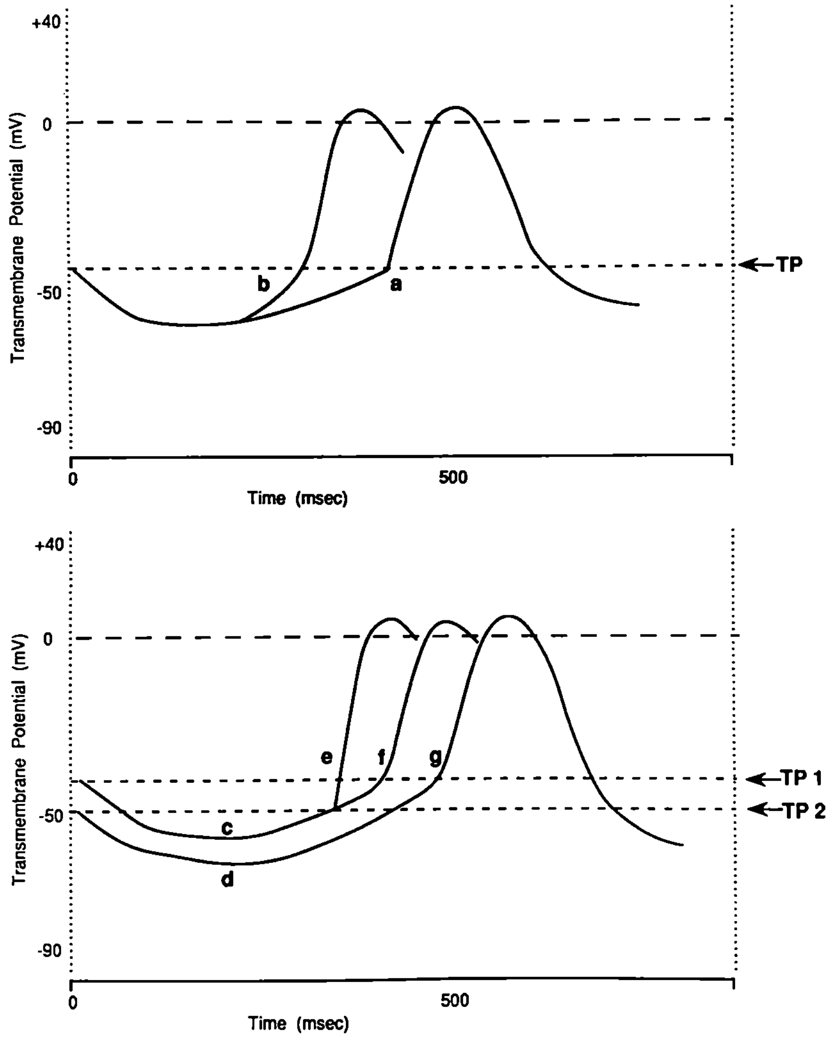


Figure 2. Mechanisms for increased automaticity. (*Top*) When threshold potential (TP) and maximum diastolic potential (MDP) are the same, an increase in the slope of spontaneous phase 4 depolarization from a to b will increase automaticity and, therefore, the rate of discharge. (*Bottom*) When MDP is the same (*c*) but the TP is changed from TP 1 to TP 2, the rate of discharge is faster (*f* to *e*). When the TP is the same (TP 1) but the MDP is made more negative (from *c* to *d*), the discharge rate will increase (from *g* to *f*).

for the Wolff-Parkinson-White syndrome. Wolff-Parkinson-White syndrome manifests as a short PR interval, and delta waves on the ECG during sinus rhythm in a patient with paroxysmal tachycardias. "Nodoventricular" or "nodofascicular" (Mahaim fibers) can produce a delta wave and may be involved in tachyarrhythmias. Slowing or block of conduction can occur at any point in the activation sequence, from SA node exit block to subtle degrees of regional intraventricular conduction delay. Further processes that participate in altered conduction are discussed.

Loss of Membrane Potential. As previously mentioned, when the resting membrane potential is less negative, fewer Na^+ channels or only Ca^{++} channels, are available for phase-0 depolarization. When fewer Na^+ channels are activated in the AP, the maximum phase-0 upstroke velocity, called Vmax, is reduced. A reduced Vmax decreases the speed of conduction. Loss of membrane potential (LMP) is not likely to be a uniform process due to varying depression of the fast response among different fibers. When heterogeneity of conduction is widespread, unidirectional or bidirectional conduction blockade can result. These conduction changes tend to favor the development of re-entrant arrhythmias, as we shall see. Common causes for this include elevated blood catecholamines, increased extracellular K^+, ischemia, or digitalis excess.

Re-entry. Re-entry occurs when a wave of depolarization loops back and triggers another wave (Fig. 3). Re-entry depends on slow conduction and uneven changes in refractoriness. The final result of re-entry can be one or more premature beats or the development of a self-perpetuating tachyarrhythmia. Sources of re-entry include sites of abnormal anatomy (scar tissue, accessory paths) and/or areas with abnormal electrical properties. The slow conduction required for re-entry can occur in slow response fibers (SA or AV nodes) or depressed fast response fibers (fast fibers with their Na^+ channels inactivated so that AP upstroke is dependent on Ca^{++} current). The other condition for re-entry, uneven refractoriness, can occur at border zones between atrial tissue and the SA or AV nodes, or in surviving fibers surrounding a zone of infarction.

CLINICAL CAUSES OF ARRHYTHMIAS

Many specific mechanisms for arrhythmias can be demonstrated in cellular laboratory preparations; however, it is often not possible to determine the exact site and cause of arrhythmias in the clinical situation without resorting to invasive electrophysiologic studies. There are no clinical electrophysiologic studies of patients undergoing anesthesia and surgery done specifically to confirm arrhythmia mechanisms. However, Table 1 lists many of the possible clinical causes for intraoperative arrhythmias.

Whether or not a patient undergoing surgery or anesthesia will develop a particular arrhythmia depends on many factors.[1] It is often difficult to distinguish between the primary cause of an arrhythmia and multiple aggravating factors. It seems logical that the general preoperative condition of the patient is important. A variety of vascular, neurologic, endocrine, hepatic, pulmonary, or renal diseases may aggravate any problems owing to already compromised myocardial func-

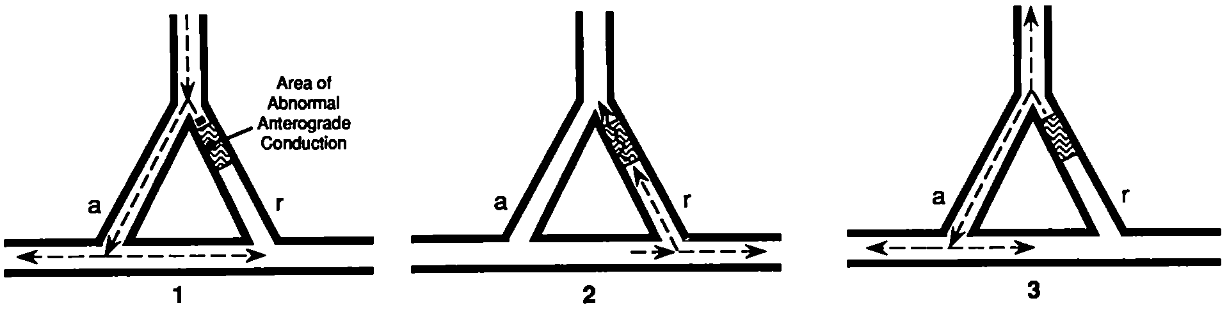


Figure 3. Mechanisms of re-entry: branching Purkinje fiber. (1) Conduction proceeds normally to the branching portion of the Purkinje fiber and continues via the forward or anterograde (*a*) path. An area of anterograde conduction block prevents the impulse from traversing down the backward or retrograde (*r*) path. (2) The anterograde impulse spreads to ventricular muscle and back up the *r* path, which is no longer refractory, and penetrates the proximal fiber through the abnormal area. (3) The *a* path has recovered from the first impulse and, if not first excited by another impulse from above, the returning impulse re-enters the anterograde path again to complete the circuit. This may occur only once or many times (sustained re-entry).

Table 1. *Causes for Intraoperative Arrhythmias*

- I. Pre-existing benign arrhythmias
  - A. Sinus arrhythmia
  - B. Athletes' bradycardia
  - C. Some ventricular ectopy
- II. Cardiac dysfunction
  - A. Impaired myocardial O_2 supply
    - 1. Low PaO_2
    - 2. Low blood O_2 carrying capacity
    - 3. Hypoperfusion (CAD, emboli, low BP)
    - 4. Cellular poisons (cyanide)
  - B. Cell death, trauma
    - 1. Trauma (accidents, surgical, etc.)
    - 2. Infarction
    - 3. Inadequate myocardial protection during cardiopulmonary bypass
    - 4. Reperfusion after coronary occlusion
  - C. Inflammation (myocarditis)
    - 1. Infections
    - 2. Immunologic
    - 3. "Catecholamine myocarditis"
  - D. Specific cardiac abnormalities
    - 1. Degenerative (Lev's, Lenegre's)
    - 2. Congenital abnormalities (congenital heart disease, pre-excitation syndromes)
    - 3. Acquired valvular heart disease (including mitral valve prolapse)
    - 4. Right and left ventricular cardiomyopathies
    - 5. Long QT syndromes (congenital; electrolyte, metabolic, or drug-induced)
    - 6. Tumors
- III. Metabolic and endocrine disorders
  - A. Starvation states
  - B. Hypermetabolism (high fever, malignant hyperthermia, neurolept malignant syndrome, hyperthyroidism)
  - C. Hypometabolism (hypothermia, myxedema)
  - D. Hyperbilirubinemia
  - E. Hyperparathyroidism
  - F. Neuroendocrine-producing tumors (eg, pheochromocytoma)
- IV. Acid-base and electrolyte disorders
  - A. High K^+ levels (renal failure, K^+ sparing diuretics, administering bank blood rapidly, release of vascular clamps [peripheral and aortic surgery, liver transplant reperfusion], rapid K^+ repletion)
  - B. Low K^+ levels (starvation, diuretics, GI losses, insulin)
  - C. High Mg^{++}, low Mg^{++} levels
  - D. High Ca^{++}, low Ca^{++} levels
  - E. Acidosis, alkalosis
  - F. Hypercarbia, hypocarbia
- V. Electromechanical cardiac stimulation
  - A. Surgical manipulation
  - B. Intravascular catheter induced (CVP catheter or wire, PA catheter)
  - C. Atrial or ventricular stretch (increased volume)
  - D. Macroshock, microshock conditions
  - E. Pacemaker induced (inappropriate discharge, malfunction, electrocautery reprogramming, or sensory evoked potential induced)
  - F. "R on T" phenomena
  - G. Extracorporeal shock wave lithotripsy
  - H. Malfunctioning automated implantable cardioverter/defibrillator
  - I. External cardioversion or defibrillation induced

Table continued on opposite page

Table 1. *(Continued)*

VI. Autonomic imbalance
  A. Sympathetic nervous system activation
    1. Surgical stimulation with inadequate anesthesia
    2. Reflex activation with decreased blood pressure
    3. Airway manipulation with inadequate anesthesia
    4. Excessive anxiety
    5. CNS injury
    6. Electroconvulsive therapy induced (2° to CNS effects)
    7. Other nervous system pathology (epilepsy, Guilliaume-Barre, tetanus, etc.)
    8. Myocardial ischemia (especially anterior)
  B. Sympathetic NS inactivation (high spinal or epidural anesthesia, bilateral stellate ganglion blocks)
  C. Parasympathetic activation (oculocardiac reflex, GI or thoracic structure traction, carotid artery manipulation, airway manipulation, ECT, inferior myocardial ischemia)
VII. Drugs
  A. Wrong drug given
  B. Absolute or relative drug overdose
  C. Idiosyncratic or allergic drug reaction
  D. Drug interactions: pharmacokinetic or pharmacodynamic
  E. Specific drugs
    1. Anesthetics
      a) Local anesthetics (especially bupivacaine)
      b) Intravenous anesthetics (ketamine, opiates, barbiturates)
      c) Volatile anesthetics (halothane, enflurane, isoflurane)
    2. Muscle relaxants (succinylcholine, pancuronium, gallamine)
    3. Proarrhythmic effects of antiarrhythmic drugs (eg, long QT)
    4. Digitalis toxicity
    5. Catecholamine or sympathomimetic induced
    6. Calcium entry blockers
    7. Beta-adrenergic blockers
    8. Cholinergic or anticholinergic drugs
    9. Respiratory drugs (aminophylline, beta-agonists)
    10. Tocolytics, oxytocics (ritodrine and other beta-agonists; ergots, pitocin)
    11. Chemotherapeutic agents (daunorubicin, doxorubicin)
    12. Psychoactive drugs (monoamine oxidase inhibitors, tricyclic antidepressants, Li^+, phenothiazines, butyrophenones)
    13. Histamine (H_2) blockers (cimetidine, ranitidine, famotidine?)
    14. Respiratory stimulants (naloxone, doxapram)
  F. Substance abuse (nicotine, amphetamines, cocaine, caffeine)
VIII. Pseudoarrhythmias
  A. Inaccurate ECG interpretation
  B. Artifact from extracardiac electrical signals

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tion. Different anesthetic techniques can profoundly affect the cardiovascular and autonomic system; the care and expertise of the anesthesiologist in selecting an anesthetic, administering the anesthetic, and maintaining physiologic homeostasis is important. For example, providing inadequate anesthesia or allowing wide swings in acid-base or electrolyte levels may promote the occurrence of arrhythmias, as discussed later.

A discussion of all disorders causing arrhythmias is beyond the scope of this review; however, some interesting or frequent etiologies from Table 1 are described.

Benign Causes

If one assumes that the normal rhythm of the heart should always be a regular, sinus mechanism with a rate between 60 and 100 beats per minute (in adults), then arrhythmias are very common, even outside the perioperative period. Abnormal rhythms may be found in 40 to 75 per cent of normal persons during continuous ambulatory ECG monitoring.[4, 36] There is no reason to suspect that these patients are at any increased risk for undergoing anesthesia. A specific arrhythmia, sinus rhythm with an RR interval varying with respiration on the ECG (so-called sinus arrhythmia), is common in healthy young adults. Also, athletic or very fit individuals commonly have heart rates that, at rest, can be in the low 40s owing to elevated vagal tone. Further, it is not unusual to occasionally encounter otherwise healthy, asymptomatic, young patients who have frequent, sometimes complex, ventricular ectopy. At least one study has documented a lack of significant adverse events in long-term follow-up of such patients.[19] There are, however, no controlled outcome studies for this type of patient undergoing anesthesia. Unfortunately, there is no way to totally rule out significant cardiac disease in every patient with a preoperative arrhythmia. However, a careful history and physical examination coupled with prudent testing should identify the vast majority of patients with arrhythmias associated with important cardiac or systemic disorders.

Cardiac Dysfunction

Myocardial cell damage or death will cause problems with the specialized electrical conduction system and myofibril pumping functions. This may, in turn, produce arrhythmias. Also, structural abnormalities of the conducting system, muscle, or valves can lead to rhythm problems. The following discussion highlights some of these causes.

Cellular Hypoxia. The effects of cellular hypoxia can be profound, whether due to decreased oxygen transport to cardiac cells from reduced O_2 carrying capacity, lowered PaO_2, or reduced perfusion. Because the maintenance of ion gradients and cellular work require fuel, a lack of high energy sources from oxidative metabolism will disrupt normal function. As K^+ leaves and Na^+ enters the cell, the transmembrane potential becomes less negative. This loss of membrane potential can generate areas dependent on slow Ca^{++} depolarization, with slowed conduction, enhanced automaticity, and greater dispersion of refractory periods. Also involved may be the production of intracellular acidosis, an increase in intracellular calcium ions, and the local release of catecholamines or other mediators. Any of these changes could promote abnormal atrial or ventricular rhythms. As all anesthesiologists are aware, the onset of sudden, profound bradycardia may be the hallmark of acute global hypoxia. Localized areas whose oxygen demand outstrips supply (as in coronary artery disease) may be the focus for almost any arrhythmia. Typically, areas of myocardial cell death from coronary occlusion or trauma are surrounded by a "penumbra" of damaged but potentially viable cells. These areas of death and near death are sources for abnormal automaticity and re-entry as discussed previously. A potent source of arrhythmias is "reperfusion" injury, which occurs with spontaneous resolution of coronary occlusion or with induced reopening during transluminal angioplasty and thrombolysis. The cause of this is not clear, but multiple mechanisms are thought to play a role.[17] Interestingly, although we shall see that volatile anesthetics can be the source of arrhythmias, in the canine model at least, they may actually reduce the incidence of these reperfusion arrhythmias.[22]

Patients who have active myocarditis from any cause are at risk for ventricular arrhythmias, as are those with dilated cardiomyopathies and abnormal valves.[21] A valvular abnormality worth specific mention is mitral valve prolapse (MVP). Prolapse of the mitral valve is a very common finding in the general population; perhaps 10 per cent or more may have this diagnosed on echocardiography. The vast majority have no symptoms or demonstrable arrhythmias.[15] Some, however, have atypical chest discomfort and may have, most commonly, premature atrial or ventricular beats. The most common symptomatic sustained arrhythmia is paroxysmal supraventricular tachycardia, although a few may have bouts of life-threatening ventricular arrhythmias.[39] Owing to the fact that most patients with MVP are not aware of their condition (nor are the anesthesiologists who care for them), it is difficult to say what is the specific risk during the perioperative period. However, if the patient is in a subgroup with documented symptoms or signs, arrhythmias may be a concern.[2, 20]

An interesting group of disorders that may produce life-threatening arrhythmias are those that produce long QT intervals on the ECG.[30] These include congenital and acquired forms. The acquired forms are associated with, among others, various drugs (as described later), hypokalemia, central and autonomic nervous system dysfunction, and MVP. When the QT interval is prolonged, myocardial refractoriness is prolonged. The resulting dispersion of recovery from a depolarization increases the likelihood of re-entrant rhythms such as ventricular tachycardia or fibrillation.[3, 12]

Metabolic or Endocrine Disorders

Derangements in body homeostasis might be expected to play inciting or modulating effects in the genesis of arrhythmias. Some do this indirectly by altering plasma concentrations of nutrients or electrolytes. Starved patients, especially those on high protein diets or those with anorexia nervosa, may have sudden death from arrhythmias related, in large part, to low plasma K^+ levels. In addition, fasting in rats has been reported to also lower the epinephrine dose needed to produce halothane-associated arrhythmias.[29]

Hypermetabolic states greatly increase the work of the heart and also cause sympathetic activation. This promotes the development of sinus tachycardia and abnormal automaticity. At the opposite extreme, hypometabolism can be a potential problem. Severe hypothermia from exposing skin and body cavities to cold operating rooms, the administration of cold intravenous fluids, and impaired thermoregulatory ability under anesthesia results in reduced SA-node automaticity, and in increased ventricular irritability, usually when core temperatures drop below 32°C.

Other examples of metabolic or endocrine problems include increased vagal tone and resulting bradycardia with high plasma bilirubin levels, arrhythmias with severe hypercalcemia in hyperparathyroidism, and tachyarrhythmias during operations to remove neuroendocrine substance secreting tumors (for example, pheochromocytoma).

Electrolyte and Acid-Base Disorders

Potassium. The effect of altered extracellular potassium ($[K^+]e$) concentrations on the genesis of arrhythmias have been a hotly debated topic. There is no question that changes in $[K^+]e$ can produce a variety of atrial and ventricular premature beats, tachycardias, or block.[31] It is apparent, however, that $[K^+]e$ is not the whole story. In fact, that ratio of intracellular to extracellular K^+ determines most of the transmembrane potential. It may not be the absolute change in $[K^+]e$ that is important, but the time course of the change. The faster the change, the less likely there has been time to equilibrate and bring the transmembrane potential toward normal. Chronic, stable changes may be less prone to provoke arrhythmias.[1, 13, 45]

Patients can develop hypokalemia from acute alkalosis, starvation, diuretics (the most common cause), insulin administration, or from $beta_2$ sympathomimetic drugs. Hypokalemia from these causes has traditionally been a major concern in the decision to proceed with an anesthetic. At least two recent studies have argued that it is logical to reduce reliance on the absolute value preoperative K^+ levels.[13, 45] It appears that dogmatic adherence to a set K^+ level as being "safe" is not appropriate and that, instead, decisions should be based on the urgency of the procedure, the time course of the K^+ change, and the overall condition of the patient, especially concomitantly administered drugs.[1] On the other hand, this more recent evidence should not be used to proceed with elective surgery when there are clear indications of severe arrhythmias that may be amenable to correction with K^+ administration. It must be kept in mind, however, that there is danger of hyperkalemia following the injudicious rapid IV administration of K^+. Suppression of normal (and abnormal) automaticity and the production of AV-conduction block and ventricular fibrillation (probably from re-entry) can result from acute increases in potassium levels. Other ways of producing rapid rises in plasma K^+ include the rapid administration of old bank blood (especially in infants), sudden surgical limb or organ reperfusion, and the use of succinylcholine in patients who have extramyojunctional spread of nicotinic receptors (patients with burns, neurologic disorders, and so forth).[37]

Other Electrolytes. Abnormal levels of other ions may promote arrhythmias in certain circumstances. Severe hypermagnesemia, usually iatrogenic, can produce AV and intraventricular conduction block, but only at concentrations above that producing respiratory arrest.[1] Recently, however, more attention has been focused on the arrhythmic potential of hypomagnesemia. Hypomagnesemia, usually in association with hypokalemia or digitalis toxicity, has been implicated in the genesis of life-threatening ventricular arrhythmias.[47] Patients who have become hypokalemic from diuretics may also become hypomagnesemic. However, the role of low Mg^{++} levels in the genesis of arrhythmias is unclear, since Mg^{++} administration has an antiarrhythmic effect, even at normal plasma levels.[40] Hypercalcemia or hypocalcemia are probably not important in producing serious arrhythmias except with large, perhaps acute, changes. The use of digoxin is often mentioned as a contraindication to calcium administration. This admonition may or may not have clinical relevance. There is no definite laboratory or clinical evidence to support not giving Ca^{++} in the presence of *nontoxic* levels of digitalis. All the often-quoted clinical reports are very old and no new ones have been published in the last 40 years.[38] At least during cardiac surgery, giving calcium in the presence of digoxin seems a common practice. There are no studies showing that alterations in plasma Na^+ are directly associated with abnormal rhythms. Lithium is often used to treat psychiatric disorders. Since Li^+ mimics Na^+ and accumulates in the cardiac cell, the resting membrane potential becomes less negative. This could impair conduction or increase ventricular irritability.[41]

Acid Base. It is probable that many primary changes in acid-base balance affect the heart through secondary changes in electrolytes and via alterations in sympathetic tone. This is especially true with carbon dioxide. Increases in CO_2 will cause intracellular and extracellular acidosis and reflex increases in blood catecholamines.[33] Decreases in CO_2, as with overzealous mechanical ventilation, can decrease both ionized Ca^{++} and $[K^+]e$.[10] Profound acidosis during severe organ hypoperfusion (lactic acid), malignant hyperthermia (CO_2 and lactic acid), and ketoacidosis are so often associated with other derangements in body function that it can be difficult to separate out all the factors responsible for arrhythmias.

Electromechanical Cardiac Stimulation

The heart produces electrical currents and, as a consequence of excitation-contraction coupling, myofibril shortening. Conversely, the heart can be affected by external electromechanical stimuli and by stretching the conducting system or muscle. These stimuli may trigger arrhythmias or, in the case of stretching and dilatation, produce reentry paths. Direct surgical manipulation of the heart is a well-known cause of arrhythmias, but one out of the direct control of anesthesiologists.[5] For example, cardiac or thoracic surgery can cause more intraoperative and postoperative rhythm disturbances than, say, a peripheral orthopedic procedure. Especially during dissection of cardiac structures or placement of cardiopulmonary bypass cannulae, atrial or ventricular arrhythmias are common.[5]

Electromechanical stimulation of the heart during insertion of central venous catheters can be the cause for various arrhythmias. Usually, care is taken to control how catheters or wires are inserted into the central veins, but during the insertion of transvenous pulmonary artery catheters, isolated or sustained ventricular beats are common.[8] Pulmonary artery catheters can also be the cause of transient right bundle branch block, which, in the presence of existing left bundle block, can result in asystole.

Premature beats or sustained abnormal rhythms may be due to microshock or macroshock hazards present in the operating suite, especially in the presence of intravascular conductive paths from catheters or wires. Pacemakers may malfunction and cause arrhythmias, usually from intrinsic problems, but they may also be inhibited by skeletal muscle or caused to undergo bizarre reprogramming from external stimuli, such as electrocautery interference.[9] Even remote stimuli from extracorporeal shock wave lithotripsy and sensory-evoked potential devices have been reported to produce arrhythmias.[28]

Autonomic Imbalance

Autonomic imbalance is an important and frequent cause of arrhythmias in the perioperative setting. Excessive predominance of either the sympathetic or parasympathetic systems can produce either rapid or slow rhythms, respectively. Sympathetic activation will occur, for example, in the presence of (1) manipulation of the airway during light anesthesia; (2) surgical stimulation during light anesthesia; (3) extreme anxiety; (4) myocardial ischemia (especially anterior); or (5) baroreflex activation from decreases in blood pressure. Interestingly, certain nervous system injuries or pathology (for example, tetanus) may cause autonomic imbalance and arrhythmias directly or as secondary effects from so-called "catecholamine myocarditis."[42] Parasympathetic predominance may occur with (1) manipulation of the airway during light anesthesia; (2) fright (vagotonic faint); (3) surgical traction on the eye and gastrointestinal or thoracic structures; (4) carotid (baroreceptor) stimulation; (5) sympathetic blockade from regional anesthesia; and (6) some instances of inferior myocardial ischemia. Some stimuli can cause both intense sympathetic and parasympathetic reactions (for example, electroconvulsive therapy).[34]

Drugs

Drugs can have many effects that, ultimately, can produce arrhythmias. Alteration of the cardiac conduction system can occur via actions directly on membranes, by acting on receptors bound to membranes, or by altering intracellular processes. Changing blood pressure will produce baroreceptor changes as well as affecting cardiac work and perfusion. Any of these effects might be explained on the basis of known drug actions. Other effects may be difficult to predict; these include problems arising from giving the wrong drug, giving too much drug, idiosyncratic reactions, and ill-defined drug interactions. Some of the known effects for specific drugs of interest to the anesthesiologist are described in the following sections.

Inhalation Anesthetics. Current evidence, at least from canine models, indicates that halothane suppresses both normal and abnormal forms of automaticity.[44] It may also promote re-entry by slowing conduction or affecting refractoriness.[44] Despite concerns about halothane's effect of depressing the SA node and decreasing AV conduction, it seems that, in normal hearts in normal conditions, and without other drug effects, clinically significant AV-conduction block or bradycardia is unlikely to be a problem.[1] However, the occurrence of slow sinus rates and competing or escape AV junctional rhythms with any of the currently used volatile anesthetics is common. Resulting loss of the atrial "kick" may be hemodynamically significant in patients with poor left ventricle compliance. However, modulation of the direct anesthetic effects on automaticity and conduction by autonomic reflex effects may lead to unpredictable results in man. For example, it is well known clinically that isoflurane anesthesia is often accompanied by increases in heart rate, especially in young people. Nitrous oxide produces a mild increase in sympathetic activity but no other specific effects on cardiac rhythm are known. By themselves, these inhalation anesthetics should probably not be considered arrhythmic; however, in the presence of cardiac disorders or other drugs, they may contribute to arrhythmias.[1] Interestingly, there is recent experimental evidence that the volatile anesthetics might actually antagonize arrhythmias by affecting transmembrane Ca^{++} flow and could be antiarrhythmic, particularly in ischemic hearts.[22, 24, 44]

Epinephrine Interactions. Some volatile hydrocarbon anesthetics can reduce the dose of catecholamines needed to provoke ventricular arrhythmias. It is widely quoted that the dose of epinephrine needed to produce ventricular premature beats in half of patients is 2.1 μg per kg for halothane, 6.7 μg per kg for isoflurane, and 10.9 μg per kg for enflurane.[16] Further, it appears that the addition of at least 0.5 per cent lidocaine to epinephrine can increase the minimum dose needed to produce ventricular premature beats with halothane from 1.3 to 2.5 μg per kg.[16] Although the epinephrine dose-response curves from this same study were steeply sigmoidal for both halothane and isoflurane, the curve for enflurane was flatter. The latter indicates that caution is necessary in assuming that epinephrine doses below 10 μg per kg are safe with enflurane. Finally, estimation of a safe dose for exogenous epinephrine with any anesthetic agent or technique will be difficult because of multiple modulating factors in any given patient. For example, there is clinical evidence that far higher doses of epinephrine are tolerated in children and, also, large amounts are routinely used topically for burn debridements.[26, 27] Moreover, there is ample evidence from animal studies that intravenous anesthetics and other drugs can modify anesthetic-epinephrine interactions to produce arrhythmias.[1] Intravenous induction agents such as thiopental, thiamylal, and ketamine (but not etomidate) may increase the sensitivity to catecholamines, but interactions in man are not well documented.[1] Other drugs including succinylcholine, cocaine, tricyclic antidepressants, monoamine oxidase inhibitors, and aminophylline (methylxanthines) promote anesthetic-epinephrine arrhythmias, especially after *acute* administration.[1] In contrast, modest doses of most local anesthetics (Na^+ channel blockers), prazosin ($alpha_1$ blocker), $beta_1$ blockers, and diltiazem or verapamil (calcium entry blockers) may have the opposite effect and reduce the number of ventricular premature beats in certain circumstances.[1]

Local Anesthetics. It is thought that local anesthetics act to block nerve conduction by binding to the inactive state of the sodium channel. As might be expected, the primary action of local anesthetics on the *heart* is to affect the Na^+-dependent fast fibers. Although local anesthetics exhibit specific affinity for Na^+ channels, there seems to be considerable variation among them in Na^+ channel binding affinities.[6, 18] Large molecules, such as bupivacaine, appear to rapidly bind to Na^+ channels but slowly dissociate ("fast in, slow out").[6] On the other hand, smaller molecules, such as lidocaine, bind quickly but also dissociate quickly ("fast in, fast out"). It is theorized, then, that bupivacaine is more likely to accumulate and cause variable degrees of conduction block and serious ventricular arrhythmias. Further, bupivacaine, by virtue of its mode of action, appears more likely to cause cardiac toxicity in overdose situations. Additionally, either hypoxia or acidosis, which depolarize the membrane, will favor even tighter binding and accumulation.

Other Drugs. Unfortunately, it seems that many of the causes for intraoperative arrhythmias are interventions that were originally intended to benefit the patient. This is not to say that all of these iatrogenic causes are preventable or foreseeable. Certainly, we can guess at the theoretic possibilities of an intervention, in any given patient, based on published reports or on the known pharmacologic properties of a particular drug. This is true with the administration of drugs that can increase parasympathetic tone (narcotics, acetylcholinesterase inhibitors, succinylmonocholine) or decrease it (pancuronium, gallamine, anticholinergics). Likewise, we know the effects of drugs that can increase sympathetic tone (methylxanthines, ketamine, naloxone, sympathomimetics) or decrease it (alpha- or beta-adrenergic blockers, CNS $alpha_2$ stimulants). It seems reasonable to be wary of the interaction of those drugs associated with elevated sympathetic activity and anesthetics that lower the threshold for epinephrine arrhythmias. Strangely, some drugs, intended as antiarrhythmics, can actually *promote* arrhythmias by producing unwanted decreases in SA-node automaticity or increased conduction blockade.[43] Also, by prolonging the QT interval, some drugs (for example, quinidine, disopyramide, amiodarone, and others) can predispose to the development of a polymorphic ventricular tachycardia also known as torsade de pointes.[35] Other drugs (antipsychotics and antidepressants, among others) as well as electrolyte abnormalities (reduced blood K^+,

Ca^{++}, or Mg^{++} levels) can prolong the QT interval and cause torsade de pointes.

The occurrence of multiple drug interactions, either pharmacodynamic (for example, halothane and epinephrine) or pharmacokinetic (for example, verapamil or quinidine's effects to raise digoxin levels), in patients taking a variety of drugs can make possible consequences unpredictable. Adding to possible confusion, there can be wide variations in the response to drugs among patients, or even in the same patient at different times.

Patients who self-administer drugs such as caffeine, alcohol, nicotine, and cocaine, to mention just a few, are increasingly common. These may produce complex drug interactions, especially with the autonomic nervous system, and may produce tachyarrhythmias.

Pseudoarrhythmias

When is an arrhythmia not an arrhythmia? When it is a pseudoarrhythmia. Among the causes for pseudoarrhythmias is the common misinterpretation of external artifact on the ECG as a rhythm disorder. Muscle artifact, loose ECG lead connections, movement of ECG lead wires, and even stray signals from intravenous infusion devices or fluid warmers may simulate arrhythmias.[32] Awareness of this potential mimicry is important to avoid unnecessary or harmful treatment.

SUMMARY

We have seen how ionic mechanisms cause the genesis of the cardiac AP, which is then propagated over the specialized conduction system of the heart. Alterations in impulse generation, impulse propagation, or both can produce arrhythmias. Changes in the physiologic or metabolic status of the patient, and concurrent drug administration (including anesthetics) can increase or decrease the incidence of arrhythmias. Many arrhythmias are a result of interventions originally intended to help the patient. If a rhythm disturbance persists, and all likely inciting or aggravating factors that are amenable to modification have been corrected, specific therapy may be indicated. Before proceeding with specific therapy, four questions should be answered. First, is this arrhythmia detrimental because it fails to produce a coordinated, regular myocardial contraction required for the maintenance of perfusion pressure and cardiac output? Second, is the rhythm an "escape" rhythm and bradycardia caused by the failure of higher pacemakers or a failure of conduction? Third, is the rhythm a tachycardia and likely to contribute to myocardial ischemia? Lastly, is this rhythm likely to degenerate into, or precipitate, dangerous arrhythmias, including ventricular tachycardia and fibrillation? Answering these questions will allow one to decide whether or not to institute drug or electrical (pacing, DC cardioversion/defibrillation) therapy. In order to choose the best treatment, it is imperative that the clinician be familiar with the underlying mechanisms and possible etiologies for the arrhythmias.

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Recognition and Treatment of Ectopic Beats

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The art of palpating the pulse and its relationship to the heart dates to antiquity. According to the Edwin Smith Surgical Papyrus,[21] the Egyptians during the Pyramid Age (3000 to 2500 BC) recognized and counted the pulse. The Ebers Papyrus indicates that this information was employed to evaluate the status of the heart.

Pienchiao, who lived in the sixth or fifth century BC is believed to be the originator of Chinese pulse-lore. According to pulse-lore,[15] a person with an intermittent pulse had his pulse counted for 50 beats. A single "intermission" after 50 beats was thought to be compatible with health. However, an intermission after 40, 30, 20, or 10 beats indicated that 1, 2, 3, or 4 internal organs "were deprived of vital air" and that death would follow in 4, 3, 2, or 1 year(s). Also, the pulse alone was considered a significant foundation for a diagnosis of the nature and location of disease.

The most influential of the Greek physicians was Galen (132 to 201 AD).[10] His tenets on the intermittent pulse became medical doctrine and remained so into the late 19th century. Galen regarded the "dropped beat" as a very serious symptom. He believed that men in the prime of life would not recover from the suspension of even a single beat and this could result in sudden death. He further stated that the dropping of a single beat or a slightly longer interval of quiescence was commonly associated with recovery from illness in older patients and children. He also recognized that the heart could add an extra beat at irregular intervals and felt this indicated disease.

The Galenic view of associating a poor prognosis in patients with an "intermittent pulse" persisted with many physicians until the 20th century. By 1900, the accurate diagnosis of several arrhythmias was made with the ink-writing polygraph, which inscribed the radial arterial and jugular venous pulsations. The views of Mackenzie, Lewis,

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and Osler had described all extrasystoles as essentially innocent. In the 1912 edition of *Clinical Disorders of Heart Beat*, Thomas Lewis discusses bigeminy (pulsus bigeminus):

> It may be said, therefore, that in themselves premature beats cannot be regarded as evidence of serious involvement of the heart-muscle, although such involvement is often found in conjunction with them . . . While premature contractions have unquestionably a relatively insignificant import, as compared to many forms of cardiac irregularity, entire neglect of their presence is not advisable.[13]

A 1969 study[7] resurrected the Galenic viewpoint about the severity of dropped beats. In this study, the entire population of Tecumseh, Michigan was observed between 1959 and 1965. Forty-five sudden deaths were recorded in this group. An association was made between ventricular premature beats on the resting electrocardiogram (ECG) and sudden death. Reanalysis of these data indicated that a universally poor prognosis need not be attached to all persons with ventricular premature beats without other signs of cardiac disease.[5] Those at highest risk for sudden death are patients with frequent complex ventricular ectopy in association with myocardial infarction, congestive heart failure, and other structural cardiac disease.

MECHANISMS OF ECTOPIC BEAT FORMATION

The specific mechanisms involved in the generation of ectopic beats are fundamental to the development of specific antiarrhythmic therapy (Table 1). Researchers have gained a greater insight into the etiology of ectopic rhythms over the past several years in the areas of abnormal automaticity and triggered activity.[12] Determination of the mechanism is helpful in the therapy of supraventricular ectopic beats; sinus node and atrioventricular (AV) node re-entry are responsive to calcium blockers, while automatic rhythms from the atrial and AV node are not as responsive to calcium blockers. Moreover, there are

Table 1. *Classification of Mechanisms of Ectopic Beat Formation*

A. Impulse generation
    Normal automaticity
    Abnormal automaticity
    Triggered activity
        Early after-depolarizations
        Delayed after-depolarization

B. Impulse conduction
    Re-entry
    Reflection

C. Simultaneous abnormalities of impulse generation and conduction
    Parasystole

definite clues on an ECG that help the anesthesiologist differentiate supraventricular re-entry from automaticity (discussed later). Determination of the mechanism in ventricular arrhythmias is difficult clinically, and therapy remains largely empiric. However, knowledge of likely clinical settings that correspond to certain mechanisms may lead to proper therapy for that mechanism.

Normal Automaticity

Normal automaticity with inherent diastolic depolarization is a property of the sinus node, atrial conduction fibers, areas of the AV-nodal complex, and the His Purkinje system. The rate of automatic depolarization decreases from the sinus node to the Purkinje system, thus all lower automatic cells are generally suppressed and are usually not responsible for ectopic beats but for escape rhythms. However, at lower heart rates and with enhanced intrinsic or extrinsic sympathetic stimulation, it is possible for a normal automatic cell to depolarize prior to being overdrive-suppressed by a higher automatic focus, resulting in an ectopic complex. An extremely anxious or maximally sympathetically stimulated patient receiving a high-dose narcotic anesthetic resulting in bradycardia would fulfill this criteria for normal automaticity-induced ectopic beats.

Abnormal Automaticity

The characteristics of the action potential can be changed by cardiac disease, drug effect, or electrolyte effects.[11, 12] Theoretically, reduction in the threshold potential to a more negative value, increasing the rate of rise of phase 4 (spontaneous diastolic depolarization), and increasing the maximum diastolic potential (resting membrane potential) to a less negative value may lead to enhanced automaticity (Fig. 1). It appears that a less negative resting membrane potential may be the most important of these effects. Less negative membrane potentials have been found in atrial cells in patients with rheumatic and congenital heart disease and in ventricular cells in areas of ischemia and infarction.[9] When the membrane potential reaches -60 mV, spontaneous depolarization may occur in atrial or ventricular fibers or Purkinje cells, probably through activation of the slow Ca^{++} channels.

Triggered Automaticity

A triggered ectopic beat differs from a truly automatic beat by requiring a preceding action potential for its generation. This activity, occurring after depolarization is complete, may occur during phase 3 of repolarization and is called an early after-depolarization, or may occur after repolarization is complete during phase 4 and is called a delayed after-depolarization (Fig. 2).

Early after-depolarizations are thought to occur because of change in K^+ movement out of the cell during repolarization or to a permeability change to Na^+ or Ca^{++} movement into the cell. These action potential changes have been induced under a variety of conditions

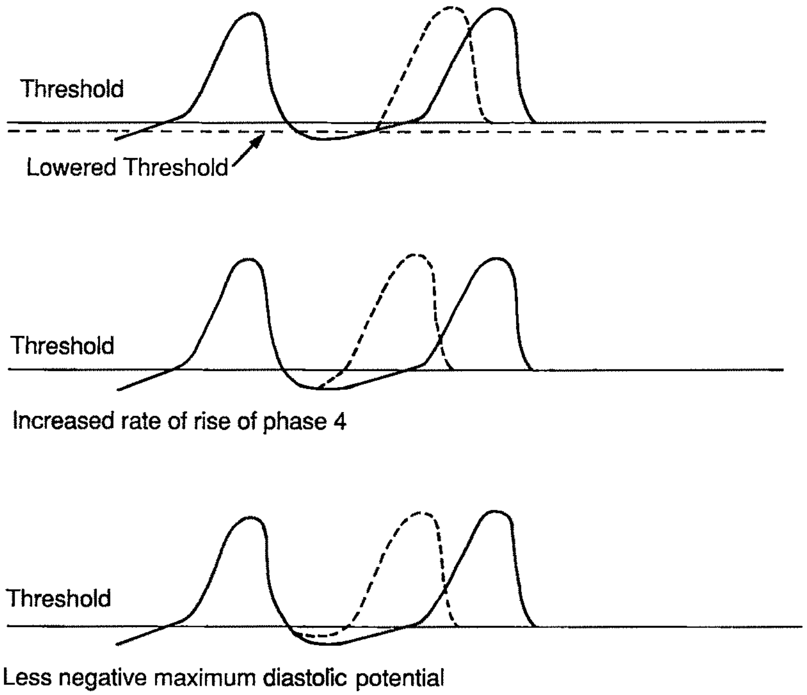
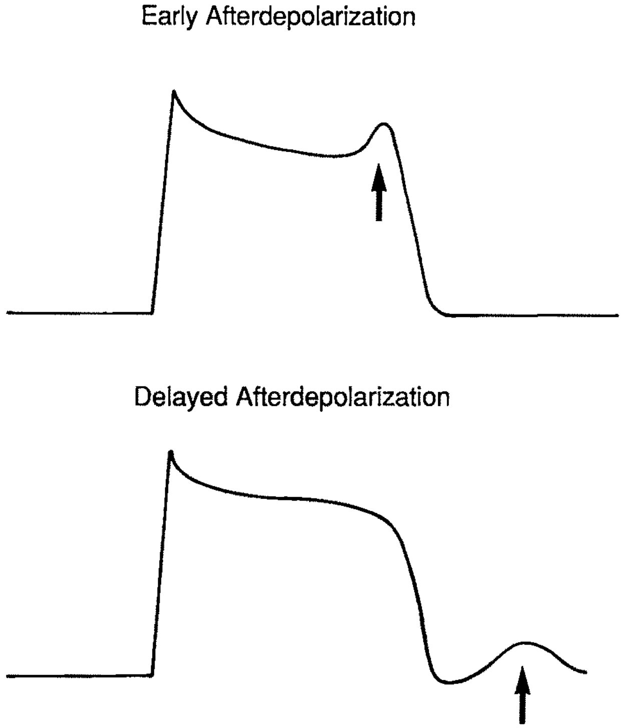

Threshold
Lowered Threshold
Threshold
Increased rate of rise of phase 4
Threshold
Less negative maximum diastolic potential

Figure 1. Basic changes in normal electrophysiology of cardiac conducting cells such as lowered threshold potential (*top panel*), increased rate of rise of phase 4 of the action potential (*middle panel*), and the presence of a less negative resting membrane potential (*lower panel*) may result in the generation of an ectopic impulse.

including hypokalemia, high concentrations of catecholamines, acidosis, hypoxia, and drugs that prolong repolarization like quinidine and procainamide.[9] Early after-depolarizations also appear more likely during slow heart rates and are probably responsible for ventricular arrhythmias in the prolonged QT syndrome (torsade de pointes).

Delayed after-depolarizations appear primarily mediated by increases in intracellular Ca^{++}. This can occur by inhibition of the Na^{+}-K^{+} pump (digitalis and hypomagnesemia), an increased serum Ca^{++}, stimulation of receptor-operated channels (catecholamines), and failure to pump Ca^{++} out of the cell (ischemia).[9] Delayed after-depolarizations have been demonstrated in normal canine coronary sinus tissue, atrial tissue from diseased hearts, ventricular specialized conducting tissue, and from normal and diseased hearts exposed to toxic concentrations of digitalis.[9] Signal-averaged electrocardiography, a computer-based process that eliminates nonrepeating random noise and averages multiple samples of repetitive waveforms, has demonstrated these "late potentials" in patients with ventricular tachycardia.[6]



Early Afterdepolarization

Delayed Afterdepolarization

Figure 2. Triggered activity. The top action potential shows an abnormal stimulus (*arrow*) during phase 3 of repolarization. This depolarizing stimulus is called an early after-depolarization. The bottom action potential demonstrates a depolarizing current (*arrow*) after repolarization is complete, a late after-depolarization. Etiology of these after-depolarizations are discussed in the text.

Re-entry

Re-entry is the classic mechanism of ectopic beat formation. There are prerequisites for re-entry: an available circuit, a difference in refractory periods of two limbs of the circuit, and conduction somewhere in the circuit sufficiently slow to allow the remainder of the circuit to recover responsiveness.[18]

Normally, the conducting impulse of the heart driven by sinus rhythm dies out after sequential activation of the atria and ventricles because it is surrounded by refractory tissue that it has recently excited. But in disease states, differences in refractoriness of tissue and slow conduction may be present, setting up a perfect substrate for re-entry formation. This is especially true in Purkinje fibers because of their arborization in the distal conducting system of the ventricle, setting up a perfect anatomic network for re-entry.

Larger anatomic circuits may exist in the sinus node, AV node, accessory pathways, vena cavae, and ventricular aneurysms that can lead to re-entry. The prototypical example of re-entry is patients with pre-excitation syndromes, using atrial muscle, the AV node, ventricular muscle, and the accessory pathway for the re-entry circuit. The AV node also demonstrates dual pathways with different refractory periods and conduction velocities that may lead to re-entry ectopic beat formation.[23]

Reflection

Reflection is a form of re-entry that occurs in a single fiber and does not require a distinct, circuitous loop as in classic re-entry. Reflection may occur because of abnormal refractoriness of adjacent areas in an individual Purkinje fiber. This process, termed longitudinal dissociation, essentially isolates areas of conducting tissue with different refractoriness, potentially allowing recovered tissue to reexcite.[22] Reflection is also thought to occur in areas of ischemic and possibly infarcted conducting tissue that can transmit depolarizing current (functioning as a passive conduit) without depolarizing. When excitable tissue is reached, depolarization may again occur, with a return of the depolarizing current across this inexcitable segment to re-excite the conducting tissue that originated the depolarizing current.

Parasystole

A parasystole is usually a ventricular automatic focus caused by either normal automaticity, abnormal automaticity, or triggered activity. This ectopic focus resists overdrive suppression from higher pacemaker cells with greater intrinsic rates. This requires some form of protection surrounding the parasystolic focus, possibly caused by a unidirectional block, an entrance but not exit block.[19] This allows the parasystole to exit and depolarize the ventricles without allowing depolarization currents to enter and to suppress it. Occasionally, there may be forms of exit block that cause the parasystole to be intermittent. Therefore, a parasystole represents abnormal impulse generation associated with abnormal conduction.

RECOGNITION OF ECTOPIC BEATS

Accurate diagnosis by the anesthesiologist is essential in the management of ectopic beats. This requires a long rhythm strip recording of lead II and, if possible, a 12-lead ECG or rhythm strips of other leads during the perioperative period. Occasionally, an esophageal lead or intracardiac electrogram may add additional information. After adequate tracings are obtained, the following approach to diagnosis is helpful in determining the etiology of ectopic beats during surgery:

1. Arrhythmia history of the patient is taken. A patient with premature atrial contractions is most likely to have the same cardiac rhythm disturbance during surgery.
2. Operative setting of the rhythm disturbance is noted. Operations near atrial or ventricular chambers may result in ectopic beats from the structures being manipulated.

3. The dominant cardiac rhythm is determined. Presumed premature ectopic beats may actually be irregular atrial fibrillation.
4. The presence or absence of P waves, preceding or following the ectopic beat is noted. Upright P waves preceding the QRS complex indicates a supraventricular ectopic beat, usually from an atrial focus. An inverted P wave preceding or following the QRS complex suggests an AV nodal origin to the ectopic beat. Always search for P waves in the T waves.
5. The width of the QRS complex is determined and compared to the normal QRS. A narrow (normal) QRS complex suggests an atrial or AV-nodal origin, and a wide (> 0.14 seconds), bizarre QRS complex suggests a ventricular origin of the ectopic beat. Aberrant ventricular conduction from a premature supraventricular ectopic beat results in a wide QRS (> 0.12 seconds) and must be distinguished from premature ventricular complexes.

In most settings ectopic beats are premature or occur earlier in the cardiac cycle than the normal sinus beats. The following discussion should aid the anesthesiologist in the recognition of premature atrial, nodal, and ventricular complexes.

RECOGNITION OF ATRIAL AND NODAL ECTOPIC BEATS

Premature Atrial Contractions

The origin of supraventricular tachyarrhythmias such as paroxysmal supraventricular tachycardia, atrial fibrillation, and atrial flutter usually is the premature atrial contraction (PAC), with either intraatrial or AV-nodal re-entry or abnormal automaticity being the likely mechanisms (Fig. 3). The key to diagnosis of PACs is locating the P wave. Lead II or V_1 is usually best for P wave determination. Depending on the degree of prematurity of the atrial contraction, the P wave may occasionally be located within the T wave, slightly altering the basic T-wave morphology (Fig. 4). The shape of the P wave is

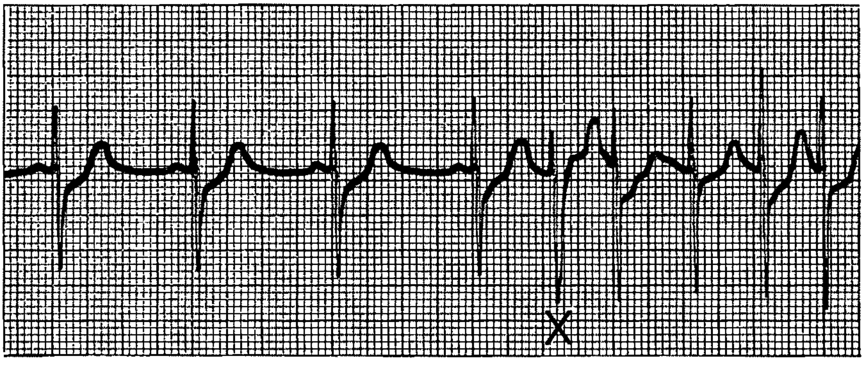


Figure 3. A PAC (*X*) resulting in atrial fibrillation. Notice the slightly larger T wave indicating a P wave buried within. Also, the QRS of the premature complex is abnormal, demonstrating aberrant ventricular conduction.

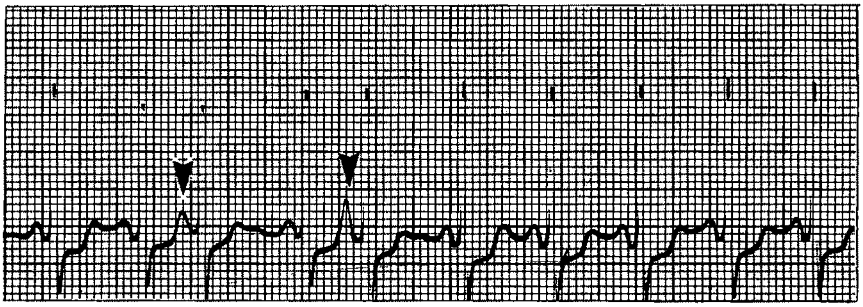


Figure 4. The arrows represent PACs, with the P waves altering the preceding T-wave morphology.

usually different than the sinus P wave, being almost identical when the premature focus is near the sinus node, or being inverted when the focus is near the atrioventricular groove.

The origin of PACs may be either right or left atrial tissue and because the spread of atrial depolarization proceeds in all directions, the sinus node is usually depolarized prematurely and reset to the intrinsic sinus rate. Therefore, the interval following the PAC is equal to the intrinsic PP interval of the sinus rhythm. This is termed a *noncompensatory pause.* Occasionally, a PAC occurring late in diastole may activate the atria milliseconds before the sinus node activates the atria, resulting in an atrial fusion beat. Therefore, the sinus node would not be depolarized (the intrinsic rhythm is not disturbed) or reset, and the pause following the PAC would be fully *compensatory*, meaning that the interval from the sinus beat preceding the PAC to the sinus beat following the PAC is twice the normal sinus rhythm interval. This occurs more commonly with premature ventricular complexes (Fig. 5).

The interval from the sinus P wave to the ectopic sinus P wave is called the *coupling interval* (see Fig. 5). Usually, this interval is constant when the PAC is occurring from a constant atrial focus, but different when several foci are involved. PACs from different foci result in varying P-wave morphology and coupling intervals and varying PR intervals owing to the varying length of time required for depolarization to spread to the AV node. The classic example of this physiology is represented in multifocal atrial tachycardia, which almost continuously suppresses the sinus node and results in a tachycardia with multiple P-wave morphologies, varying PR intervals, and a totally irregular rhythm (Fig. 6).

The QRS complex with PACs usually appears narrow or normal, representing conduction through the AV node to the bundle branches and Purkinje fibers. However, as the degree of prematurity of a PAC increases, the pathway taken through the intraventricular conduction system may become abnormal or *aberrant*[20] (see Fig. 4). Normal repolarization of the ventricular conducting system occurs in a para-

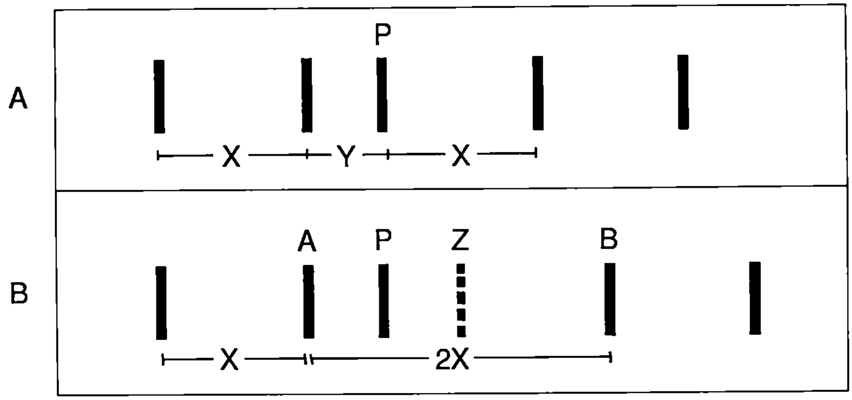


Figure 5. (*A*) The premature beat (*P*) causes a reset of the sinus node, with the following pause (*X*) being equal to the intrinsic sinus rate. Y represents the coupling interval of this premature beat. (*B*) The premature beat (*P*) prevents the normal sinus depolarization from capturing the ventricle, QRS (Z). The pause following the premature beat is a compensatory pause because the interval from the preceding sinus beat (*A*) to the following sinus beat (*B*) is twice the intrinsic RR interval.

doxical manner; the last to depolarize is frequently the first to repolarize. This is explained in part by varying action potential durations, with the proximal bundle branches having longer action potentials than more distal elements. The most proximal portion of the right bundle branch is usually the last part of the ventricular conduction system to repolarize. If the prematurity of a PAC is such that the depolarization of the ventricular conduction system occurs when the right bundle branch is still in a state of repolarization, the conduction will proceed down the left bundle, yielding a QRS complex resembling a right bundle branch block (Fig. 7). This is the most common pattern of aberrant ventricular conduction and results in an abnormal

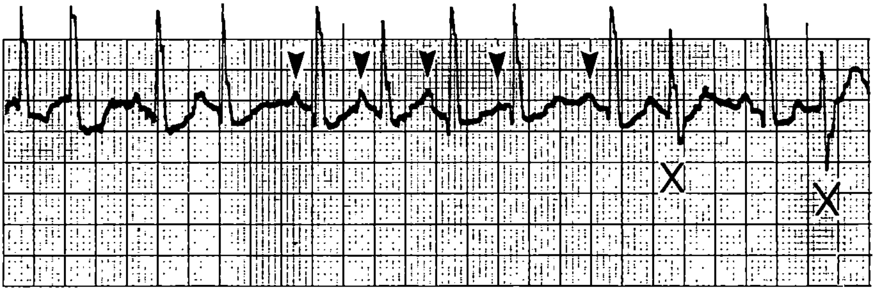


Figure 6. Multifocal atrial tachycardia. Notice the totally irregular rhythm, the varying morphology of the P waves (*arrows*), and the varying PR intervals. The two beats marked X represent aberrant ventricular conduction with QRS morphology (RBBB pattern) different from the normal QRS.

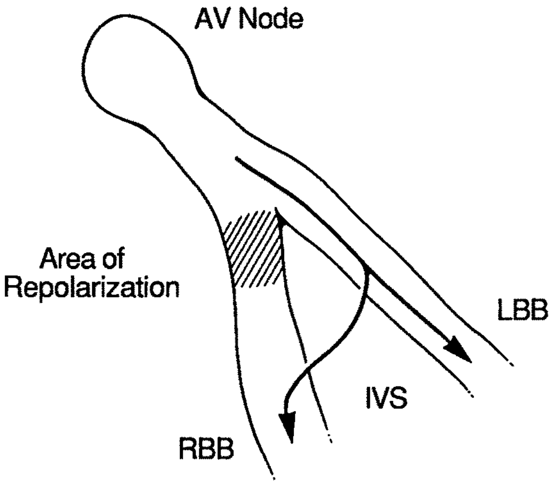


Figure 7. Aberrant ventricular conduction. With the proximal portion of the right bundle branch (*RBB*) being the last part of the conducting system to repolarize, a PAC depolarization wave enters the left bundle branch (*LBB*) and spreads across the interventricular septum (*IVS*), giving the QRS complex the configuration of a right bundle branch block.

or wide QRS complex. However, in a small percentage of patients, the proximal left bundle branch is the last to repolarize, resulting in a left bundle branch block pattern, when aberrancy results from a premature supraventricular complex. This is more frequently associated with cardiac disease, whereas right bundle aberrancy is usually physiologic.

The greater the prematurity of ectopic beats, the greater the degree of aberrancy, resulting in many different QRS morphologies. The presence of cardiac disease, cardiac and noncardiac drugs, and electrolyte problems may all affect the contour of the QRS complex in aberrancy. Occasionally, in the same patient, the aberrant QRS complexes may differ. Thus, it is important to distinguish these multiple morphologies of the QRS complex in aberrancy from the wide QRS complex of premature ventricular complexes. Table 2 lists some distinguishing features of aberrantly conducted premature supraventricular complexes and premature ventricular complexes.

The degree of prematurity required to result in aberrant ventricular conduction varies with the heart rate and the immediately preceding cycle length (Fig. 8). Because repolarization times are shorter at faster rates than slower rates, greater prematurity is required during faster rates for aberrancy. In atrial fibrillation there is a totally irregular rhythm. Repolarization times also are totally irregular because they depend on the preceding RR interval, which is variable. Therefore, a QRS complex following a long RR interval will have a longer repolarization time, providing a greater likelihood for an aberrantly con-

Table 2. *Differences in Aberrantly Conducted Premature Atrial Complexes and Premature Ventricular Complexes*

ABERRANT CONDUCTION (PACS)	PVCS
Preceding P waves	P waves absent
RBBB pattern common	RBBB pattern uncommon
Initial deflection of QRS identical to normal QRS	Initial QRS deflection may differ from normal
QRS width, > 0.12 sec.	QRS width > 0.14 sec.
Noncompensatory pause	Compensatory pause
In atrial fibrillation, varying coupling intervals	In atrial fibrillation, constant coupling intervals

ducted beat (Ashman phenomena), than a QRS complex following a short RR interval, which will have a much shorter repolarization time (Fig. 9).

Premature Nodal Contractions

The mechanism involved in the generation of premature nodal contractions (PNCs) may be normal or abnormal automaticity or AV-nodal re-entry. The P waves may precede the QRS complex from a high nodal focus or follow the QRS from a lower nodal or His bundle focus. Frequently, the P waves from AV nodal re-entry are buried within the QRS and are not visible (Fig. 10). If the P waves are visible, the morphology of the P waves is usually upside down or inverted in the inferior leads because the depolarization of the atria proceeds from AV node toward the SA node or in a retrograde fashion. Therefore, it is frequently difficult to distinguish a low atrial PAC from PNC with retrograde P waves.

The same rules apply for compensatory and noncompensatory pauses, coupling intervals, and aberrant ventricular conduction, following PNCs as for PACs. However, because of the distance and other anatomic structures separating the AV node and sinus node, sinus

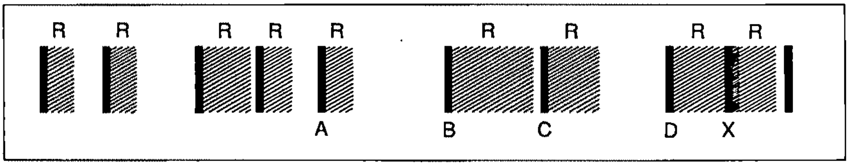


Figure 8. Atrial fibrillation with varying refractory periods (*R*). Notice the long refractory period following B due to the long preceding interval (*AB*) and the shorter refractory period following C due to the shorter RR interval (*BC*). Cardiac refractoriness is a beat-to-beat phenomenon directly dependent on the preceding RR interval. With the long interval CD, the refractory period following D is long, resulting in beat X falling within this period of refractoriness and resulting in aberrant ventricular conduction.

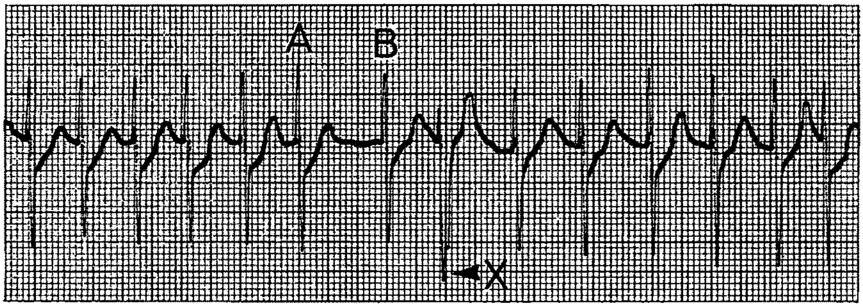


Figure 9. Atrial fibrillation with aberrancy. Notice the long interval (*AB*), which results in prolonged refractoriness after B resulting in aberrant conduction with a right bundle pattern (*X*).

node reset and noncompensatory pause are not as likely with PNCs as with PACs.

Various parasympathetic and sympathetic effects, digitalis excess, electrolyte imbalance, anesthetic effects on autonomic tone, and various cardiac disease states may produce premature nodal depolarization and nodal arrhythmias.

THERAPY FOR ATRIAL AND NODAL ECTOPIC BEATS

The main consequence of PACs and PNCs is the precipitation of supraventricular tachyarrhythmias that are frequently associated with hemodynamic and ischemic problems. The correction of electrolyte problems, autonomic imbalance, surgical manipulation, drug effects, acid-base problems, increased atrial size secondary to volume overload, and myocardial ischemia is necessary prior to the institution of specific antiarrhythmic therapy. Premature supraventricular beats are

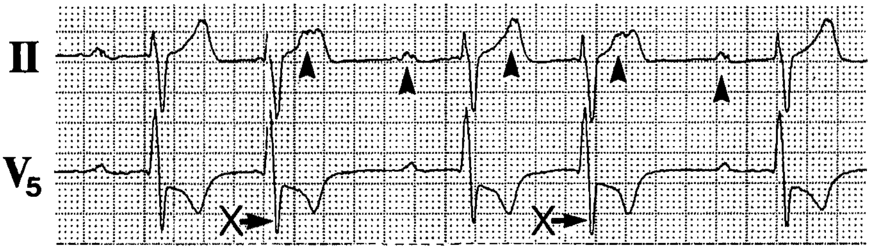


Figure 10. Premature nodal beats (*X*). The arrows indicate atrial activity with an underlying prolonged PR interval. Notice the P waves on the T waves. However, it is possible that the P wave on the T wave immediately preceding the PNC conducted with a prolonged PR interval (2:1 Wenckebach). This cannot be absolutely determined from this tracing.

more frequently associated with noncardiac causes, while PVCs are generally associated with cardiac causes.

The class IA antiarrhythmics have atrial electrophysiologic properties suitable for the treatment of premature supraventricular beats. Intravenous procainamide is suitable for the perioperative period to suppress ectopic atrial foci. Additionally, procainamide is effective in converting atrial fibrillation to sinus rhythm, further supporting its antiarrhythmic properties on atrial tissue.[8] Digitalis has been classically used in suppressing atrial arrhythmias; however, its major benefit is slowing AV-node conduction and fast ventricular response after supraventricular tachyarrhythmias arise. Beta-receptor blockers also may aid in the therapy of premature atrial beats associated with high autonomic states or increased catecholamine levels. Verapamil may be especially helpful in preventing premature nodal beats that result from AV-nodal re-entry because verapamil is very effective in converting AV-nodal re-entry supraventricular tachycardia.[14]

RECOGNITION OF PREMATURE VENTRICULAR COMPLEXES

The most common cardiac arrhythmia is premature ventricular complexes (PVCs) (Fig. 11). They can occur in healthy people during stress, anxiety, sleep, or exercise. PVCs may be precipitated by stimulants such as caffeine, alcohol, or nicotine, by therapeutic drugs, and by cardiac and noncardiac diseases.

P waves are almost never associated with PVCs although occasionally an inverted retrograde P wave may be seen following the PVC. This requires an intact retrograde pathway through the ventricular conduction system, His bundle, and AV node. The sinus node P waves are usually not seen because they are buried within the QRS of the PVC. However, late end-diastolic PVCs may occur immediately after the sinus P wave and should not be mistaken for PACs (Fig. 12).

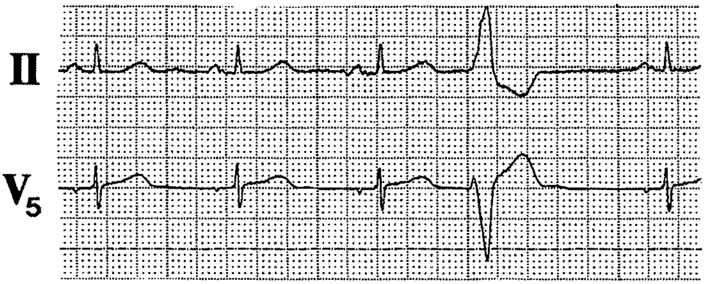


Figure 11. PVC. Notice the different morphology in different leads and the opposite polarity of the T wave. This ectopic beat has the pattern of a left bundle branch block and may originate from the right ventricle.

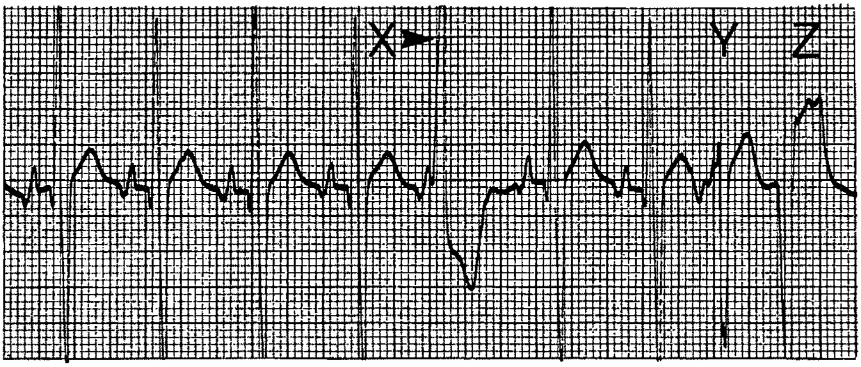


Figure 12. End-diastolic PVCs occurring immediately after the P wave (*X* and *Y*) beats Y and Z form a multifocal couplet.

Usually, the PR interval is very short, allowing insufficient time for depolarization to spread to the ventricles. End diastolic PVCs are common and are thought to occur after atrial contraction because of the increased filling and left ventricular stretch occurring with atrial systole. Interpolated PVCs are ectopic beats that do not affect the underlying sinus rhythm (Fig. 13). These beats are somehow "isolated," and the depolarization wave front does not interfere with the next sinus depolarization of the ventricles.

Rarely, the sinus node may be depolarized by the PVC and reset, resulting in a noncompensatory pause. Compensatory pauses classically are associated with PVCs (Fig. 14). The depolarization waves from atrium and ventricle meet usually in the AV-nodal region, obliterating each other and allowing the sinus node to continue its intrinsic rhythm. Therefore, the interval encompassing the PVC is equal to twice the intrinsic RR interval, a full compensatory pause.

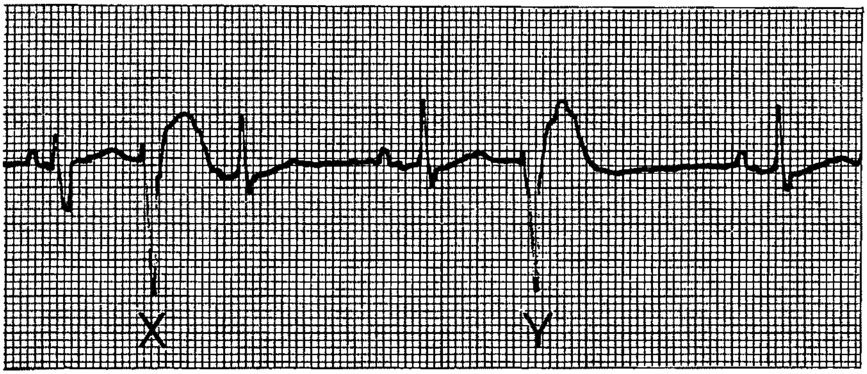


Figure 13. Interpolated PVC (*X*). Notice the failure of X to change the supraventricular rate without a pause while PVC (Y) results in a full compensatory pause.

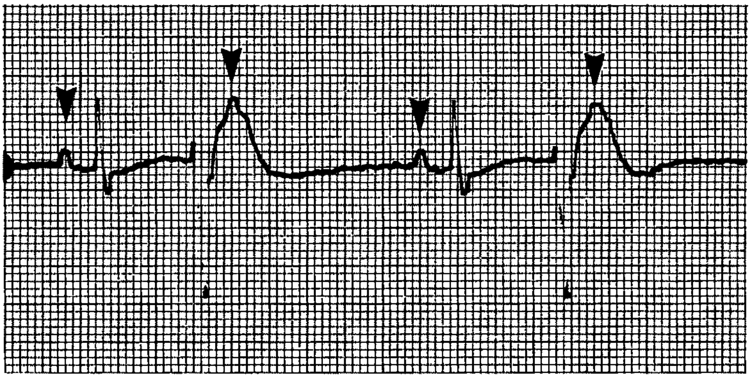


Figure 14. PVCs with compensatory pause. The arrows indicate atrial activity. Notice the P wave on the T wave of the PVC, indicating failure to reset the sinus node and the failure of that sinus impulse to capture the ventricle resulting in the compensatory pause.

The QRS complex with PVCs is usually wide (> 0.14 seconds) with varying morphology. Origins of ectopic activity from the right ventricle with early activation of the areas of the right bundle may have the appearance of a left bundle branch block and PVCs from the left ventricle may have the appearance of a right bundle branch block (Fig. 15). The widened QRS results from the slow spread of activation from the ventricular muscle to the ventricular conducting system compared with the fast depolarization through the conduction system during supraventricular controlled rhythms (Fig. 16). Occasionally, PVCs occurring high in the ventricle close to the conducting system will have a more normal appearance. Also, the QRS complex in a single lead may appear narrow and normal but appear wide and bizarre in a different lead, underscoring the importance of obtaining multiple leads in monitoring or diagnosing cardiac rhythm and rhythm distur-

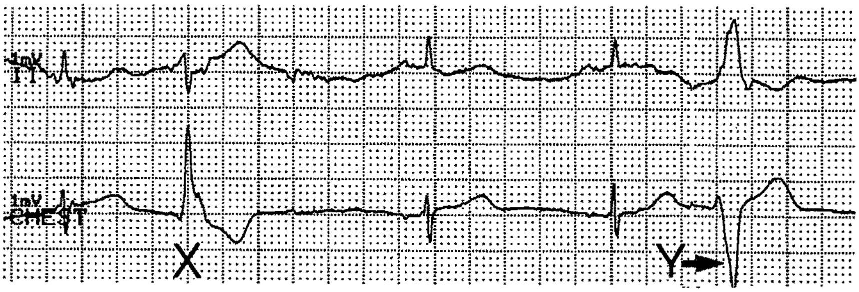


Figure 15. Multifocal PVCs with varying coupling intervals and opposite polarity. In lead II, PVC X has a right bundle pattern (left origin) and PVC Y has a left bundle pattern (right origin).

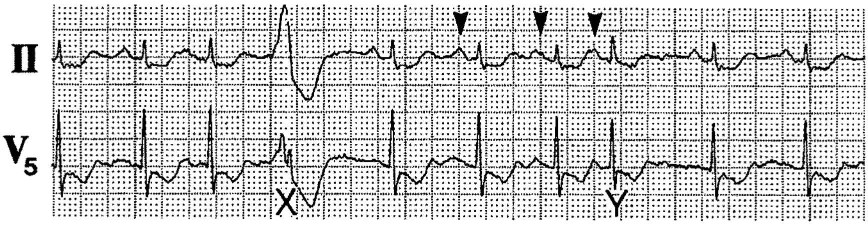


Figure 16. The wide, bizarre beat (*X*) is a PVC with a compensatory pause. The arrows represent atrial activity with beat Y, a PAC, causing sinus node reset, and a noncompensatory pause.

bances. Fusion beats may occur with end-diastolic PVCs. The normal sinus-induced depolarization of the ventricle begins and fuses with the ectopic depolarization from the PVC. The initial deflection of the QRS may appear normal but rapidly turns into a wide, bizarre pattern (Fig. 17).

Another helpful distinguishing feature of PVCs is the secondary T-wave changes that occur. Primary T-waves changes are defined as T-wave abnormalities occurring from primary cardiac disease such as ischemic heart disease. Secondary T-wave changes occur secondary to changes in depolarization of the heart, as in bundle branch blocks, left ventricular hypertrophy, and PVCs. The T waves may be more widely and deeply shaped and are usually inverted opposite the direction of the QRS complex (see Fig. 11). Occasionally, T-wave changes may occur in the sinus QRST complex following the PVC. The significance is controversial but may represent myocardial is-

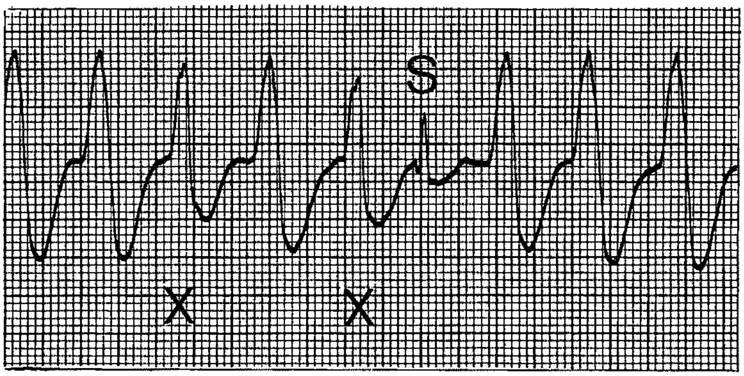


Figure 17. Fusion beats. Ventricular tachycardia is interrupted by two fusion beats (*X*) with sinus depolarization of the ventricles fusing with the ventricular ectopic activity. Note the complete sinus capture of the ventricle (*S*). Fusion beats are an important distinguishing feature of ventricular tachycardia in the diagnosis of wide complex tachycardias.

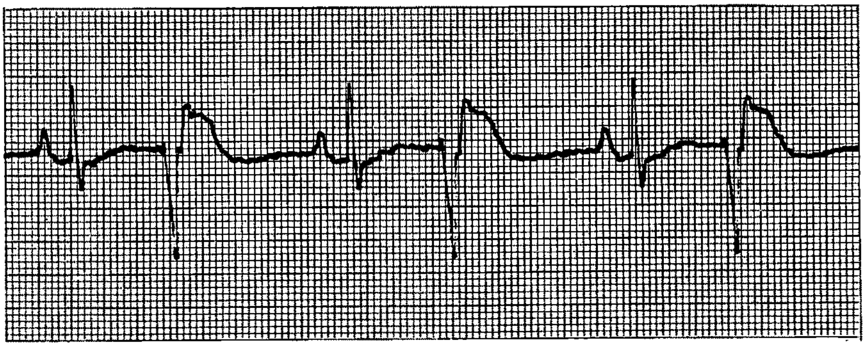


Figure 18. Unifocal PVCs in a bigeminal pattern with constant coupling intervals.

chemia. Additionally, morphologic changes may occur in the sinus P wave following a PVC that is caused by retrograde activation of the atria. The next sinus-induced atrial depolarization occurs while the atria are still in a state of repolarization, resulting in abnormal atrial depolarization pattern. This is appropriately called aberrant *atrial* conduction.

The coupling intervals of PVCs from the same ventricular focus should remain constant (Fig. 18). However, with multifocal PVCs associated with varying QRS waveforms, the coupling intervals will vary (Fig. 19). Also, coupling intervals will vary with a single parasystolic focus. A parasystole is thought to represent an automatic ventricular rhythm that is constantly present and not suppressed by the intrinsic sinus-induced ventricular complexes. Because the parasystole has a different rate than the sinus rate, it will be present at various times during diastole with a varying coupling interval, but with a single, wide QRS morphology. Parasystole usually occurs during slower heart rates and may represent the mechanism of early after-depolarization.

The classification of PVCs by Lown (Table 3) is popularly used

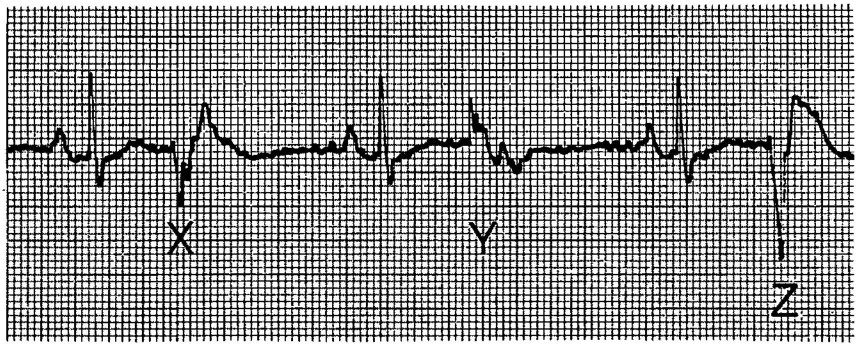


Figure 19. Multifocal PVCs (*X,Y,Z*) with varying coupling intervals.

Table 3. *Classification of PVCs (Lown)*

Class 0	None
Class 1	Less than 30/hr
Class 2	Greater than 30/hr
Class 3	Multifocal PVCs
Class 4	Repetitive (couplets or 3 or more PVCs)
Class 5	R-on-T phenomena

to define more malignant ventricular arrhythmias that are more likely to degenerate into ventricular tachycardia and fibrillation (Fig. 20). The presence of Lown class 3, 4, or 5 increases the risk of sudden death in patients *after myocardial infarction.*[17] However, increased frequency of PVCs after myocardial infarction is also associated with increased mortality.[2] The prognosis is worse for repetitive PVCs than for multifocal or R-on-T PVCs.[3] Nevertheless, and of utmost importance, the severity of the arrhythmia and its relation to the risk of anesthesia and surgery remains undefined.

THERAPY FOR VENTRICULAR ECTOPIC BEATS

Treatment of premature ventricular depolarizations requires the anesthesiologist to have an adequate knowledge of arrhythmia history, underlying organic heart disease, and prior antiarrhythmic therapy. Patients with ventricular arrhythmias can be divided into three classes based on their associated risk for sudden death.[1] *Benign ventricular arrhythmias* represent patients without structural heart disease whose risk of sudden death is minimal. These patients usually have no hemodynamic symptoms and frequently are not treated; although, if palpitations and dizziness are bothersome to the individual, therapy may be elected.

Potentially malignant ventricular arrhythmias occur in patients

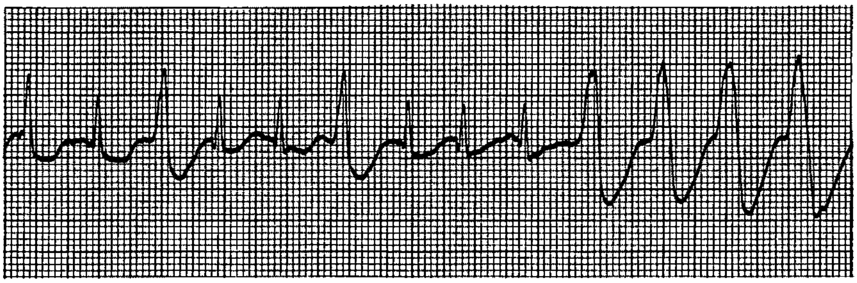


Figure 20. Unifocal PVCs during a sinus tachycardia have precipitated ventricular tachycardia. This is more likely to occur with frequent PVCs (trigeminal pattern in this patient).

with structural heart disease, those with severe coronary artery disease, a history of myocardial infarction, and those with congestive or hypertrophic cardiomyopathy, all of whom have a higher risk of sudden death than patients with no known heart disease and ventricular arrhythmias. These patients usually are receiving antiarrhythmic therapy prior to their anesthetic, and if arrhythmias arise during anesthesia and surgery, they should be treated.

The final classification, *malignant ventricular arrhythmias*, is associated with severe structural heart disease with associated hemodynamic abnormalities. These patients have symptoms of dizziness and syncope and may have a history of cardiac arrest. Most of these patients will benefit from intravenous antiarrhythmic therapy during the stress of the perioperative period, and cardiology consultation should be obtained for discussion and choice of therapy in each individual patient.

The patient with no known heart disease, with or without a history of *benign ventricular arrhythmias*, may have PVCs during anesthesia and surgery. Ventricular arrhythmias are common in the normal general population and increase with age.[4, 11] During surgery the anesthesiologist may be the first physician to monitor the patient for any prolonged length of time and may uncover these common benign arrhythmias. Therapy is usually not indicated; however, the prudent anesthesiologist should use these cardiac electrical problems as a warning that something noncardiac may be wrong, including myocardial ischemia, hypoxemia, hypercarbia, acidemia, light anesthesia, sympathetic stimulation, electrolyte abnormalities, or drug effects. If intraoperative problems arise associated with ventricular arrhythmias, however, antiarrhythmic therapy may be justified until the etiology of these problems can be determined.

In the patient with known structural heart disease, *potentially malignant ventricular arrhythmias* should be more aggressively treated. Once again, after noncardiac causes are ruled out, therapy is based on the patient's organic heart disease and any previous antiarrhythmic therapy. Any patient with ischemic heart disease with new ventricular arrhythmias must have ischemia ruled out. Intravenous nitroglycerin has frequently eliminated premature ventricular depolarizations without antiarrhythmic therapy. Patients with congestive heart failure or congestive cardiomyopathy may have worsening failure with a dilated heart, which should be managed appropriately. Worsening obstruction in hypertrophic cardiomyopathy may require volume loading with pure vasopressors like neosynephrine, beta blockade, or calcium entry blockade to help relieve the obstruction. Likewise, patients with mitral valve prolapse may also require volume loading, neosynephrine, and beta blockers to eliminate their ventricular arrhythmias. Although beta blockers are effective in mitral valve prolapse, frequently other antiarrhythmic therapy may be necessary.

When a patient with potentially malignant ventricular arrhythmia is receiving antiarrhythmic therapy prior to surgery, the patient should be questioned to see if any symptoms have been relieved. Drug levels,

Table 4. *Ventricular Antiarrhythmic Agents*

Class I	Na^+ channel-blocking drugs
IA	Moderately slows depolarization, prolongs repolarization (quinidine, procainamide, disopyramide)
IB	Mildly slows depolarization, shortens repolarization (lidocaine, mexiletine, tocainide)
IC	Markedly slows depolarization, little effect on repolarization (flecainide, encainide)

if available, should be obtained to verify adequate therapeutic levels. A cardiologist should be asked what intravenous antiarrhythmic agent is appropriate if ventricular arrhythmias occur in the operating room. The most commonly used agents for control of ventricular arrhythmias are shown in Table 4. Appropriate intravenous antiarrhythmic therapy during anesthesia should initially come from the same class as chronic oral therapy. For example, if the patient takes mexiletine or tocainide (IB), this suggests that intravenous lidocaine (IB) may be effective. However, if mexiletine or tocainide levels are adequate and lidocaine is not effective, the arrhythmia may require a different classification for combination therapy, for example, procainamide (IA) with the IB agents. If this intravenous combination is not effective, then other intravenous combinations (Table 5) may be required.

The management of patients with *malignant ventricular arrhythmias* with hemodynamic symptoms and organic heart disease is basically the same as for potentially malignant ventricular arrhythmias except the anesthesiologist and cardiologist must be more aggressive in documenting adequate therapy and in considering prophylactic therapy. Some of these patients may have automatic implantable cardiovertor defibrillator units or have had invasive or noninvasive ablative therapy for their arrhythmia. The most common organic heart problem is coronary artery disease, and ischemia is a likely precipitating cause. Prophylactic nitroglycerin with intravenous antiarrhythmia therapy and beta blockade with the usual precautions for anesthetic induction and maintenance in these patients is entirely appropriate.

Intravenous antiarrhythmic therapy begins with lidocaine, which remains a very effective agent against PVCs with minimal side effects. If lidocaine is not effective, the substitution or addition of intravenous

Table 5. *Intravenous Combination Drug Therapy*

Lidocaine	IB
Lidocaine and procainamide	IB, IA
Lidocaine, procainamide, and beta-antagonists	IB, IA, II
Lidocaine and bretylium	IB, III
Lidocaine, bretylium, and procainamide (?)	IB, III, IA

procainamide may prove effective. Procainamide is also an excellent antiarrhythmic for PVCs with efficacy similar to lidocaine and when combined with lidocaine, this combination of IA and IB drugs may be more effective than with either drug alone.[16] For refractory PVCs during the perioperative period, beta blockers are useful due to their antagonism of increased catecholamine levels that occur during stress and may play a role in the genesis of PVCs. Intravenous lidocaine (IB) and bretylium (III) also is a potentially beneficial combination for therapy of PVCs in the perioperative period (see Table 5).

SUMMARY

The recognition of ectopic beats is a necessary skill of the anesthesiologist. The significance of these beats during the perioperative period depends on the arrhythmia history of the patient, the presence or absence of organic heart disease, the operative setting with mechanical or extra-cardiac etiologies involved, and the frequency and repetitiveness of the ectopic beats. All these and other considerations are included in the decision to observe benign ectopic beats in a healthy patient or to aggressively treat more frequent ectopic beats in a patient with organic heart disease.

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Differential Diagnosis of Narrow Complex Tachycardias

*William L. Chester, MD**

Anesthesiologists must be capable of rapidly assessing, diagnosing, and treating potentially lethal arrhythmias. Tachycardias are likely the most common rhythm disorders seen in the perioperative period and often result from emotional and physical responses to anesthesia and surgery. In addition, these stresses may exacerbate existing cardiac disease or unmask underlying myocardial or conduction system abnormalities previously unknown to the patient or physician.

As our patient population becomes older we can expect to confront hemodynamically significant arrhythmias more frequently. These patients will often be less tolerant of cardiovascular stress and are more likely to incur significant morbidity.[13]

Narrow complex tachycardias (NCTs) encompass those tachyarrhythmias that produce QRS complexes with a duration of less than 0.12 msec. This implies a normal activation sequence through the atrioventricular (AV) node, the conduction system, and the ventricles, and a rate of more than 100 beats per minute for the adult. The underlying abnormalities leading to NCTs may be due to enhanced automaticity or circus movement (re-entry). NCTs most frequently originate from supraventricular foci (Table 1). The converse is not necessarily true; that is, wide complex tachycardias are not necessarily due to a ventricular focus. These are detailed in the article by Herschman and Kaufman in this issue.

The supraventricular tachycardias may be further described by their clinical presentation: either paroxysmal (sudden onset) or nonparoxysmal (gradual onset). Some of the paroxysmal forms of supraventricular tachycardias have been described as separate clinical entities (paroxysmal sinus, atrial, or junctional tachycardia) but will be grouped under the parent heading in the following discussion.

DIAGNOSIS

The cardiologist relies heavily on analysis of the 12-lead electrocardiogram (ECG) for the diagnosis of NCTs. Important electrocar-

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Table 1. *Classification of Narrow Complex Tachycardias*

- Supraventricular tachycardia
  - Sinus tachycardia
  - Atrial tachycardia
  - Multifocal atrial tachycardia
  - Atrial flutter
  - Atrial fibrillation
  - Atrioventricular junction tachycardia
- Other narrow complex tachycardias
  - Narrow complex ventricular tachycardia
  - Pseudotachycardia
  - Pre-excitation syndromes

QRS < 0.12 msec, ventricular rate > 100 beats per minute in adult.

diographic findings include the atrial rate, P-wave morphology and relationship to the QRS, ratio of atrial to ventricular depolarizations, precipitating or terminating events (for example, premature atrial depolarizations), and response to vagal maneuvers.[1, 4, 8, 9, 13, 15]

Anesthesiologists must often rely on other diagnostic aids to complement their review of isolated ECG leads in confirming a diagnosis. The integration of all data available in the operating room is essential. A 12-lead ECG is never in place during surgery. Rather, surgical patients may be monitored with a 3-, 4-, or 5-electrode ECG, providing at most 7 leads. However, patients often have arterial, central venous, or pulmonary artery catheters in place. Open-chest procedures may allow direct observation of atrial and ventricular function. Additionally, atrial or esophageal electrodes can be placed relatively easily. Integrating data from these monitors, the clinical situation, and the patient's history will aid in precise diagnosis of the arrhythmia.

The ECG should initially be used in the filtered (monitor) mode when evaluating an arrhythmia. This decreases baseline drift and attenuates ST and T waves (hence it should *not* be used to evaluate ischemic changes). Switching to the unfiltered (diagnostic) mode may then allow better determination of P-wave morphology. Increasing the oscilloscope sweep or recorder speed to 50 or 100 mm per second may reveal hidden P waves, as will increasing the gain (amplitude) of the display. Lead II should be selected because the P wave is prominent in this lead, but any lead showing good P-wave morphology will suffice initially. The origin of the atrial impulse may be determined to some extent by P-wave configuration on the surface ECG.[9]

Atrial activity can be demonstrated by connecting a saline-filled central venous pressure (CVP) catheter or the pacing leads of a pacing Swan-Ganz catheter to the ECG monitor. Maximal current leakage in intracardiac ECGs should be less than 10 μA to prevent microshock. Alternatively, an esophageal ECG may be used to diagnose a supraventricular arrhythmia. An esophageal ECG system may double the diagnostic specificity of ECG lead II and V_5 monitor system, is associated with minimal morbidity, and can be incorporated into an

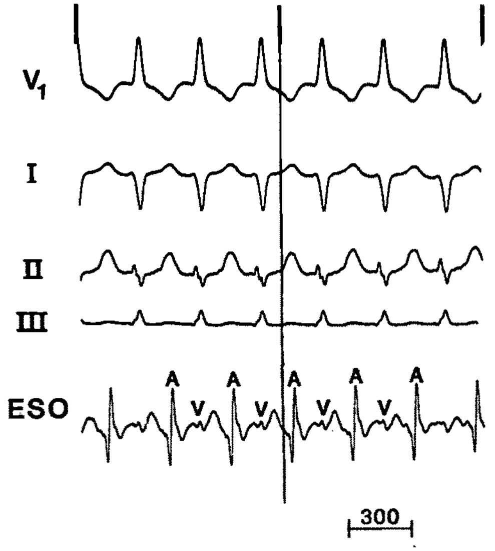

Figure 1. Esophageal ECG in a patient with atrial tachycardia. Note absence of P waves in limb and precordial leads and the presence of clearly defined atrial depolarization in the esophageal lead. (*From* Butto F, Dunnigan A, Overholt ED, et al: Transesophageal study of recurrent atrial tachycardia after baffle procedures for complete transposition of the great arteries. Am J Cardiol 57:1356, 1986; with permission.)

esophageal stethescope.[3, 6] It is especially useful in distinguishing AV nodal from atrial tachycardias, supraventricular from ventricular rhythms, and atrial flutter from fibrillation.[5] (Fig. 1).

Vascular Catheters

The arterial and CVP traces can yield a great deal of information about the contraction sequence of the heart. Loss of atrial contribution to cardiac output from asynchronous or absent atrial contraction may lead to a sudden drop in the systolic pressure (Fig. 2). The appearance of "cannon" A waves in the transduced CVP recording may indicate that the atria are contracting against closed AV valves (Figs. 3A and *B*). Here the P wave may be lost in the QRS complex (for example, in junctional tachycardias). Atrial fibrillation may be heralded by a change from a smooth arterial tracing showing only respiratory variation, to an erratic, "fuzzy" appearing trace caused by beat-to-beat variations to stroke volume as ventricular filling time changes (Fig. 4).

Direct Visualization

Direct observation of the heart in open-chest procedures is an additional method for analyzing atrial rate, contraction sequence, AV-conduction ratio, and the presence of atrial flutter vs fibrillation.

NARROW COMPLEX TACHYCARDIAS

Sinus Tachycardia

Sinus tachycardia is characterized by a rate of 100 to 180 beats per minute with 1:1 AV conduction (Fig. 5). The P waves are upright

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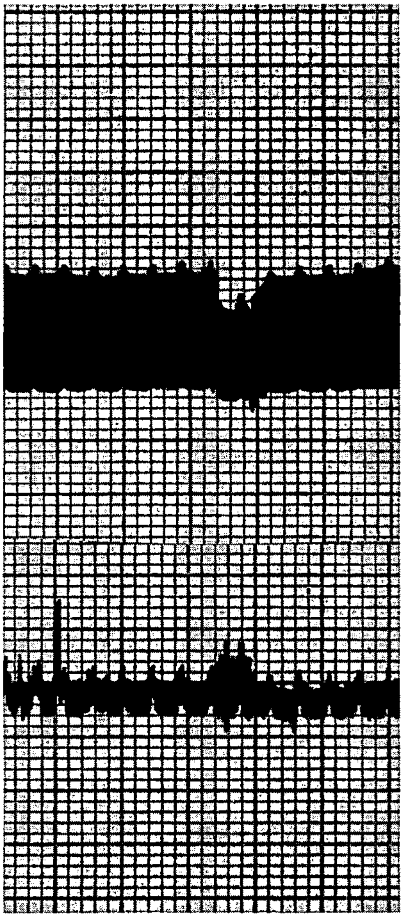

Figure 2. Arterial (*top*) and CVP (*bottom*) trend traces. Note sudden drop in arterial pressure and rise in CVP associated with a 20-second episode of junctional rhythm. (Chart speed 10 mm per minute.)

(except in lead aVR) indicating activation from the high right atrium and propagation down and to the left. P-wave morphology is uniform, PR interval is stable or may shorten with faster rates, and PP interval may vary slightly.[13] Vagal tone or beta blockade slows the rate.

Sinus tachycardia is a normal cardiovascular response to stress. It results either from increased frequency of depolarization of the sinoatrial (SA) nodal cells owing to an increase in the slope of phase 4 of the action potential or possibly from a shift to faster cells within the SA node.[4] Anything enhancing sympathetic or inhibiting vagal

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Figure 3. (*A*) Normal ECG trace (*top*) with simultaneous CVP waveform (*bottom*). Note the normal-appearing CVP waveform. (Chart speed 50 mm per second.) (*B*) Junctional rhythm (note lack of P waves in ECG trace) associated with "cannon" A waves in the CVP trace owing to simultaneous atrial and ventricular contraction. (Chart speed 50 mm per second.) *See figure on facing page.*

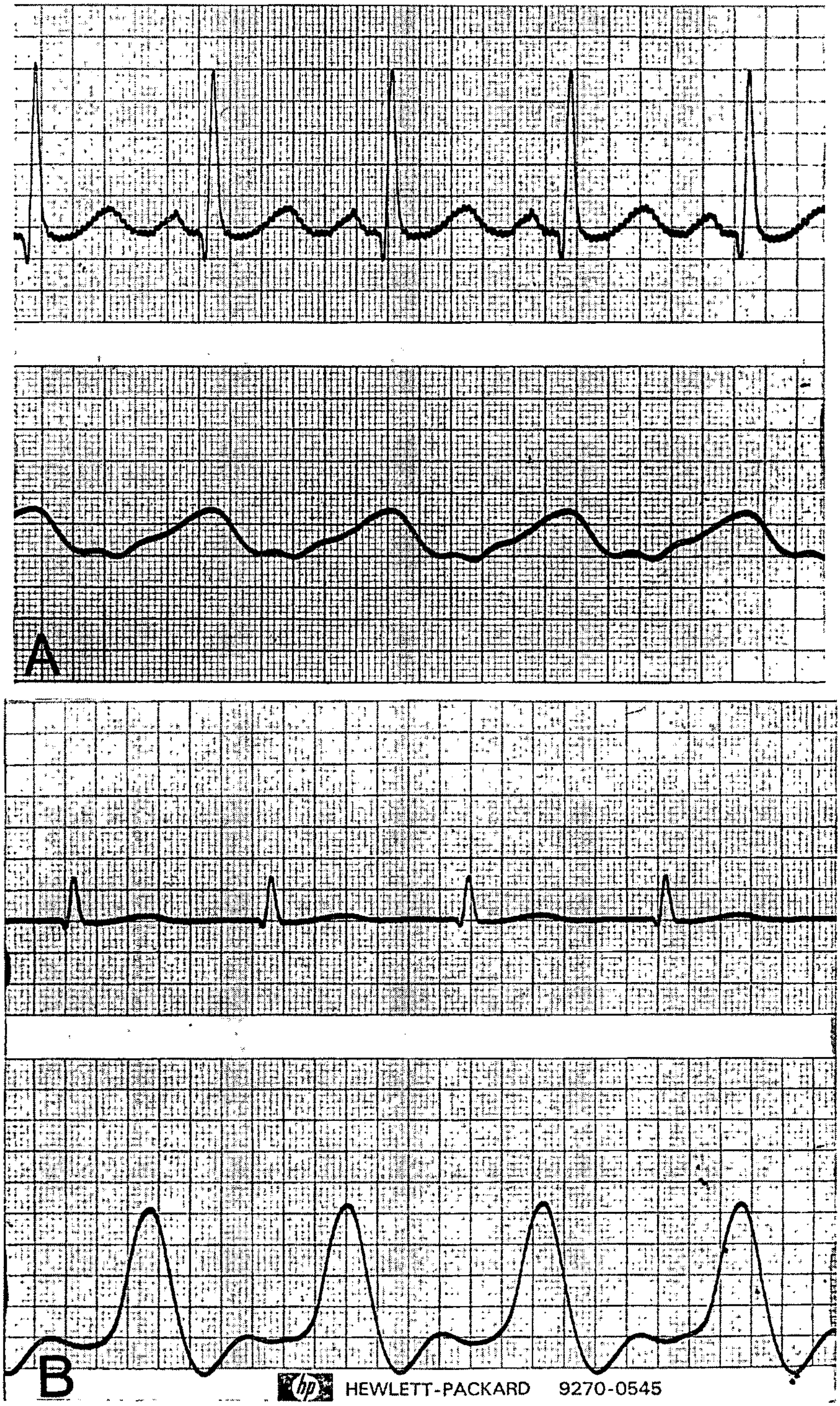

Figure 3. *A–B. See legend on facing page.*

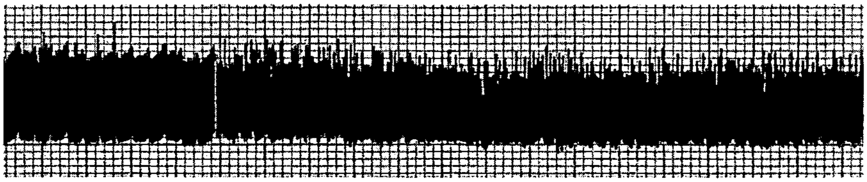

Figure 4. Arterial pressure trend trace. Note appearance of waveform during sinus rhythm at left, showing primarily respiratory fluctuations. Trend then changes to a "fuzzy," irregular appearance at arrow owing to variable ventricular stroke volume coincident with the onset of atrial fibrillation.

tone can initiate this rhythm. It is the compensatory rhythm in low cardiac output, hypermetabolic, and physiologic stress states.

Sinus tachycardia is commonly seen in anxious patients about to undergo surgery, in pediatric patients until puberty, and in pregnancy. It may be exacerbated with general or major conduction anesthesia with concomitant hypovolemia or with exogenous drug administration. During surgery it may be reflective of pain, physiologic stress, or awareness.

Once sinus tachycardia is diagnosed, a search for the underlying cause should be made and corrective measures taken. If the rhythm requires immediate control, beta blockade or cholinesterase inhibitors (edrophonium, neostigmine) will slow the rate. However, this may worsen the clinical situation if the tachycardia is compensatory (hypovolemia, congestive heart failure) or the result of the treatment of bronchospasm. Short-acting or cardioselective beta blockers (esmolol, metoprolol) may minimize adverse side effects.

Atrial Tachycardia

The atrial tachycardias seem to defy clear classification, but most authors categorize them by mechanism (enhanced focal automaticity versus re-entry) and by onset (gradual versus paroxysmal).[1] The term

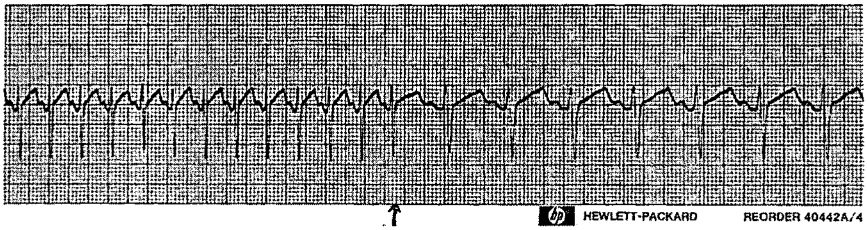

Figure 5. Normal sinus "tachycardia" in an infant. The chart speed was increased from 25 to 50 mm per second at the arrow for better definition of the P to QRS relationship.

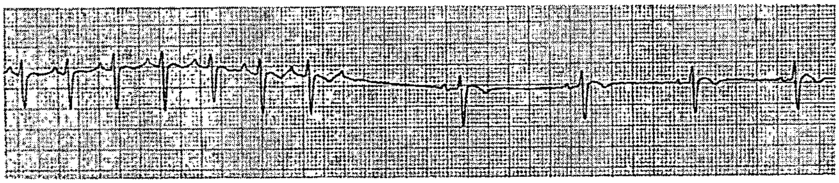

Figure 6. Atrial tachycardia. Note that the P wave is different from sinus. Termination occurs after the development of Wenckebach AV block.

atrial tachycardia will refer to any nonsinus, non-AV junctional tachycardia originating from an ectopic atrial pacemaker, either gradual or paroxysmal in onset, and arising from either automatic or re-entrant mechanisms.

The atrial rate in atrial tachycardia is 130 to 200 beats per minute (Fig. 6). Ventricular conduction is usually 1:1, but AV block may occur at high atrial rates or if the rhythm is a result of digitalis toxicity.[1] The P wave will be morphologically different from the sinus P wave and may be inverted if originating from the left or low right atrium.[9, 15] The PR interval can be short or long depending on the conduction rate and distance from the impulse generation site to the AV node.[13]

Atrial tachycardia at a rate of 150 beats per minute may be easily confused with atrial flutter with 2:1 block. Vagal tone has little or no effect on the atrial rate in either rhythm but may slow the ventricular rate by inducing AV block. This may allow visualization of either concealed flutter waves or the isoelectric segments between successive P waves typical of atrial tachycardia. Atrial or esophageal electrocardiography may also distinguish these rhythms by revealing P waves not seen in the surface ECG.[13]

The paroxysmal form of atrial tachycardia usually occurs in children or young adults and is seldom associated with underlying SA disease. Though it is sometimes used synonymously with re-entrant atrial tachycardia, paroxysmal atrial tachycardia may be either automatic or re-entrant in origin.[13] Re-entrant paroxysmal atrial tachycardia is easily interrupted with atrial pacing, which may be therapeutic as well as diagnostic.[5] Atrial tachycardia may be precipitated by sinus tachycardia or premature atrial complexes. Re-entrant forms of atrial tachycardia may terminate spontaneously, after a PAC, or by gradual slowing.[20] It can often be controlled with digitalis plus a quinidine-like antiarrhythmic (for example, disopyramide). Verapamil may be used, but is often ineffective and may actually increase the atrial rate. Amiodarone is very effective in chronic control of atrial tachycardia.[13]

There is a very high association between atrial tachycardia with AV block and digitalis toxicity.[4] When suspected, digitalis toxicity should be treated by discontinuing the digitalis preparation and normalizing potassium levels. Propranolol, phenytoin, or lidocaine are helpful if the rhythm persists.

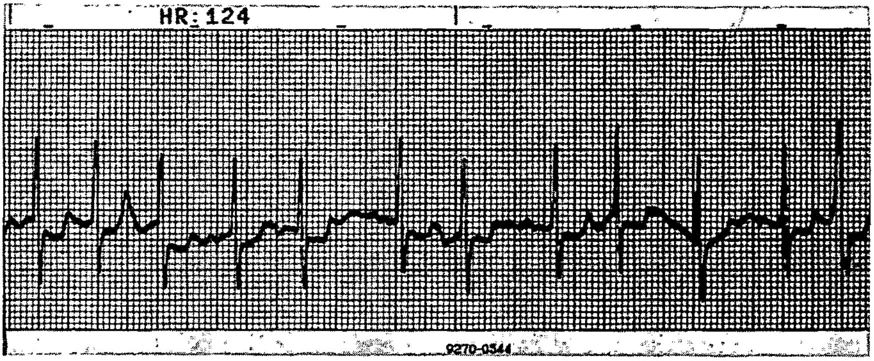

Figure 7. Multifocal (chaotic) atrial tachycardia. Note at least three different P waves, irregular PP and RR intervals, and variable PR intervals.

Multifocal (Chaotic) Atrial Tachycardia

Multifocal atrial tachycardia (MAT), by definition, originates from multiple (more than three) atrial foci. It is often a transitional arrhythmia in diseased atria that progresses to atrial fibrillation. The atrial rate is 100 to 150 beats per minute and AV conduction is usually 1:1 (Fig. 7). The P waves show variable morphology and random PP intervals because of the different initiating foci. The irregular rhythm gives the ECG a chaotic appearance difficult to distinguish from atrial fibrillation. Episodes of MAT may be interspersed with sinus rhythm.[4] MAT is thought to be precipitated by atrial disease in conjunction with an exacerbating factor (electrolyte changes, beta stimulation, fever, exercise). It is common in elderly patients with pulmonary disease, but also may occur in children.[4]

Treatment should first be directed at correction of any electrolyte abnormalities (K^+, Mg^{++}). Digoxin and quinidine, as well as verapamil, may be effective acutely. Amiodarone is effective in long-term management.[4]

Atrioventricular Junctional Tachycardia

The AV junction includes the AV node, bundle of His, and tissues immediately adjacent to these structures. Tachycardias arising in the area of the AV junction are notoriously difficult to localize and may be impossible to distinguish from other supraventricular tachycardias.[13] Good documentation of the mechanism of junctional tachycardia is often nonexistent. Classically, junctional tachycardias are NCTs without an antecedent P wave (Fig. 8). However, the P wave is quite variable as it can be located anywhere in relation to the QRS (within, after, or before). Its morphology may be normal, bifid, or inverted. This is due to the ability of a junctional impulse to travel up or down the conducting pathways, reaching atrial and ventricular tissue simultaneously. Any activation sequence is possible and will de-

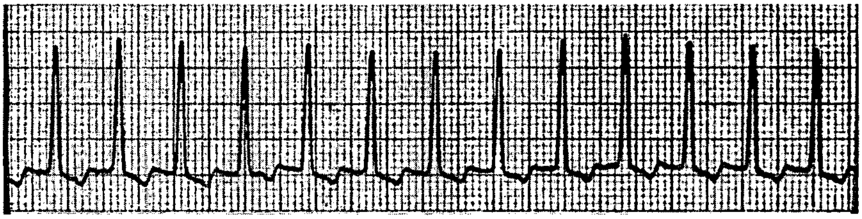

Figure 8. Atrioventricular junctional tachycardia. There are no discernible P waves, the rhythm is regular, and the rate is approximately 150 beats per minute. This is very difficult to distinguish from atrial flutter with 2:1 block.

pend on the relative conduction times of atrial and ventricular paths and the presence of block at the AV node.

The nonparoxysmal form of junctional tachycardia is most common.[13] The rate does not usually exceed 130 beats per minute. It is commonly associated with heart disease (inferior wall infarction, rheumatic fever, cardiac surgery) or digitalis toxicity. This rhythm should be suspected if atrial flutter or fibrillation changes from an irregular to regular tachycardia after digitalization.[4] Nonparoxysmal junctional tachycardia may terminate spontaneously when a faster rhythm supercedes it or after a PAC, and it is responsive to both sympathetic and vagal tone. Treatment is with digitalis (except in digitalis toxicity) or direct current countershock.

Paroxysmal junctional tachycardia is most often due to re-entry within the AV node. Patients often have no underlying heart disease but may have a history of palpitations or syncope.[21] The rate is usually between 150 and 250 beats per minute and regular. P waves are usually hidden within the QRS complex. Initiation is abrupt, often in association with a PAC, and may exhibit "warm up" like re-entrant sinus tachycardia. Increased vagal tone may slow or terminate this rhythm.

Initial treatments aim at increasing vagal tone either with drugs such as edrophonium or baroreceptor stimulation with carotid massage or phenylephrine. Alternatively, verapamil is effective in 90 per cent of cases. If these drugs are unsuccessful, digitalis, propranolol, or synchronized direct-current cardioversion may be used. Prevention of recurrent attacks can be accomplished with digitalis, disopyramide, procainamide, or quinidine.[4, 14]

Atrial Flutter

Atrial flutter has been described extensively since it was observed by MacWilliam in 1887. Lewis, in 1913, described the ECG manifestations of atrial flutter, including the "sawtooth" baseline, regular, and uniform P waves, and inverted P waves in leads II and III (Fig. 9).[10, 11] Unfortunately, atrial flutter has yet to be fully and precisely defined. Current definitions vary from "any regular atrial rhythm more than 200 bpm"[13] to detailed morphologic descriptions of the surface

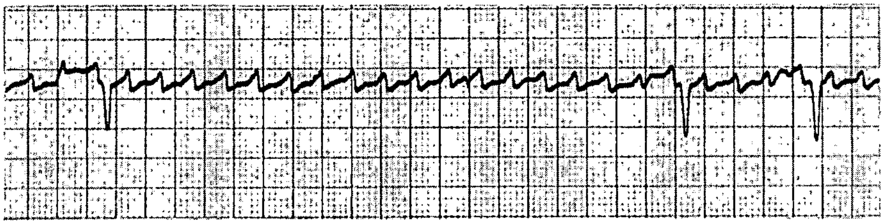

Figure 9. Atrial flutter with high-grade AV block showing typical "sawtooth" flutter (F) waves.

ECG. Some generally agreed upon characteristics are rapid and regular atrial rhythm (250 to 450 beats per minute); morphologically identical atrial depolarization waves (flutter or F waves) best seen in leads II, III, and aVF; common association with 2:1 (or greater) AV block; and frequent degeneration to atrial fibrillation or sinus rhythm. The P waves in atrial flutter are highly regular and have a characteristic undulating or sawtooth appearance in the inferior leads of the surface ECG. Clear isoelectric segments are, however, seen between distinct P waves in the atrial ECG.

A large body of experimental evidence implicates a macro-re-entrant circus movement as the cause of flutter, but focal automaticity cannot be excluded.[7, 17] One classification scheme for atrial flutter divides the rhythm into two rate groups based on the ability to change the rate and morphology of the flutter waves by overdrive pacing (that is, to entrain the rhythm).[17] Type I flutter has a rate of 240 to 340 beats per minute and is entrained by rapid pacing. This has also been called "classic" atrial flutter. Type II flutter is unaffected by rapid pacing and has a rate of 340 to 440 beats per minute. An older classification scheme uses the polarity of the flutter waves in the inferior leads to divide flutter into "common" and "uncommon" types. None of these classifications has major importance in the clinical diagnosis of atrial flutter. Atrial flutter is frequently associated with underlying myocardial disease (rheumatic fever, cardiomyopathy, ischemia), valvular heart disease, or metabolic derangements. It may also occur in paroxysmal form in otherwise normal patients.[4]

The clinical implications of atrial flutter are frequently determined by the ventricular rate response. This in turn is dependent on the refractoriness of the AV node or the presence of AV bypass tracts. Two to one block is the most common, often producing a fixed, regular ventricular rate of about 150 beats per minute. However, high-grade block, 1:1 conduction, and irregular conduction may occur. Irregular ventricular rates may reflect Wenckebach AV block or varying block in different segments of the AV node. This may mimic atrial fibrillation on the surface ECG. Enhancing vagal tone may increase AV block or convert flutter to fibrillation, often reducing the net ventricular rate.[13]

The decision on how to treat atrial flutter will depend on how severely the rhythm compromises the patient's hemodynamics. Synchronized direct-current countershock at low power settings (50 to 150 J) is often successful in converting flutter to a sinus rhythm or atrial fibrillation. Overdrive pacing may terminate type I flutter. Verapamil, digitalis, beta blockers, or anticholinesterases may slow the ventricular response enough to confirm the diagnosis (by revealing concealed F waves) or may be therapeutic by slowing ventricular rate. Quinidine, disopyramide, or procainamide may then be added to help control persistent flutter.[4]

Atrial Fibrillation

Atrial fibrillation is the rapid, uncoordinated depolarization of atrial tissue that does not result in effective mechanical contraction of the atria. It frequently results from the degeneration of other atrial tachyarrhythmias such as multifocal atrial tachycardia or atrial flutter. It often occurs in the setting of ischemia, atrial distension (valve disease, pulmonary emboli), autonomic changes, or sinus node disease.

The stresses associated with anesthesia and surgery may occasionally precipitate atrial fibrillation. Stress may occur in response to anxiety, acute pain, drugs needed in anesthetic management, or manipulation of the heart during cardiac and thoracic surgery.

Atrial fibrillation may be chronic, occur in paroxysms, or exist as a transient state between episodes of flutter or sinus rhythm. Fibrillation is described as "coarse" or "fine" depending on how well the fibrillatory (f) waves are seen on the surface ECG (Fig. 10).[2, 6]

The QRS complexes in atrial fibrillation are normally narrow since ventricular conducting pathways are unaffected. The ECG appears chaotic, with random variability in RR intervals reflecting the chance transit of atrial depolarizations through the AV node. The arterial pressure trace will show wide beat-to-beat variability owing to the variable ventricular filling times, often manifest by "fuzziness" in the trend tracing (Fig. 4). The cause of fibrillation is probably multiple re-entry circuits within the distended or diseased atrial tissue. When several different circus paths are established, the atrial contractions become uncoordinated and degenerate into fibrillation. Likewise, if the number of circus movements decreases, the fibrillatory pattern coarsens until flutter or another rhythm appears.[13]

Treatment of atrial fibrillation will again depend on the clinical situation. The hemodynamic consequences of atrial fibrillation are

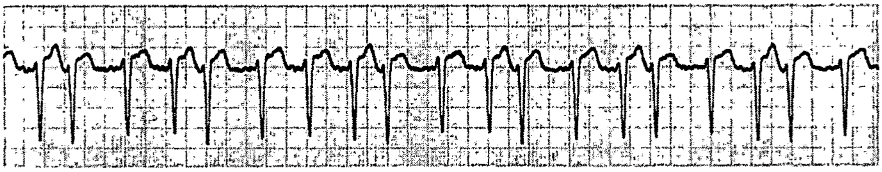

Figure 10. Atrial fibrillation. Irregular rhythm, indistinct fibrillation (f) waves.

secondary to (1) loss of atrial contribution to cardiac output and (2) high ventricular rate. Hypovolemia may exacerbate these problems and should be corrected if present. The high ventricular rate may exacerbate myocardial ischemia. Synchronized direct current cardioversion is often successful in atrial fibrillation of recent onset, and is the treatment of choice in hemodynamically significant atrial fibrillation.

Because ventricular rate in atrial fibrillation is determined by the refractoriness of the AV node, therapy is aimed at reducing AV conduction. Anticholinesterases, beta blockers, and digitalis will slow the ventricular response. Conversely, anything enhancing AV conduction (vagolytics, beta agonists, quinidine-like antiarrhythmics) can increase the ventricular rate, exacerbating hemodynamic difficulties.[18] Sudden regularization of the ventricular rhythm indicates that the underlying rhythm has changed, for example, to flutter with fixed AV block (usually 2:1) or to junctional tachycardia. This latter, as mentioned previously, may indicate digitalis toxicity.

Miscellaneous Narrow Complex Tachycardias

Pseudotachycardia. This describes a rapid ventricular rate due to the superimposition of two alternating slow rhythms. For example, a sinus rhythm at a rate of 70 may alternate with a junctional rhythm at a rate of 70 to produce an effective ventricular rate of 140. An ECG characteristic of both rhythms will be present until one pacemaker becomes dominant.

Narrow Complex Ventricular Tachycardia. The occurrence of narrow QRS tachycardia from an infranodal source has been reported during electrophysiologic studies.[19] Simultaneous activation of both bundle branches by an ectopic or re-entrant focus in the ventricular septum may produce this rhythm. Because it has only been sustained in the setting of triggered automaticity, its frequency and clinical significance are unknown.

Pre-excitation Syndromes. Wolff-Parkinson-White syndrome may occasionally present as a variant with a narrow QRS complex. Lown, Ganong, and Levine described a group of patients who were clinically similar to Wolff-Parkinson-White-syndrome patients but had normal PR intervals and narrow QRS complexes.[12] These syndromes clinically mimic AV-nodal re-entrant tachycardia and may be precipitated by a PAC or during the stress of anesthesia and surgery. They can usually be treated with verapamil or beta blockers acutely and type I antiarrhythmics (procainamide, disopyramide) chronically.[4] The pre-excitation syndromes are discussed in detail in another article in this issue.

SUMMARY

The NCTs represent a spectrum of diverse electrophysiologic and clinical arrhythmias originating anywhere from the SA node to the ventricular septum. They are due to re-entry circuits or areas of enhanced focal automaticity. Clinical history, electrocardiography, and hemodynamic data are all important contributors to the accurate diagnosis and treatment of these arrhythmias. Verapamil is effective in treating many NCTs, although digitalis, beta blockers, procainamide, or cardioversion may be required.

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Differential Diagnosis of Wide QRS Tachycardias

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The appearance of a tachycardia associated with a wide QRS complex on the electrocardiogram (ECG) monitor ($QRS \geq 0.12$ seconds) usually engenders a sympathoadrenal response on the part of the observer. Although rapid treatment may be necessary, one must quickly recall the differential diagnosis of wide QRS tachycardias (Table 1) and look for clinical or electrocardiographic clues that will aid in making the diagnosis. Misdiagnosis will lead to mistreatment, which will adversely affect the patient.[13] We review the mechanisms for development of wide QRS tachycardias, differential diagnosis of these tachycardias, discuss the etiologies of these arrhythmias, and provide general guidelines for treatment.

MECHANISMS FOR DEVELOPMENT OF WIDE QRS TACHYCARDIAS

Recalling a few facts regarding the normal progression of conduction in the His Purkinje bundles will help clarify the mechanisms for development of a wide QRS complex.

1. The normal QRS is the result of conduction of an incoming supraventricular impulse through the atrioventricular (AV) node into the His bundle, the bundle branches and Purkinje system to and through the myocardium.
2. The duration of the action potential and recovery of excitability are nonuniform throughout the His Purkinje myocardial system; repolarization and refractory periods are normally not homogeneous. As the impulse progresses away from the AV node down the His Purkinje system to the myocardium, there is an increase in the action potential duration as well as the

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Table 1. *Wide QRS Tachycardias*

SVT with pre-existing bundle branch block
SVT with aberrancy
Pre-excitation syndromes
Ventricular tachycardia
Paced ventricular rhythm
Ventricular flutter/fibrillation

refractory period until the Purkinje-myocardial junction is reached; at this point the refractory period of the myocardium decreases markedly. This concept is also very helpful in understanding the concept of re-entry.

3. The conducting system through the right ventricle (right bundle) has a more prolonged refractory period at any given level of the conduction system than does the left ventricle (left bundle).
4. The action potential duration and length of the refractory period are directly related to the length of the cardiac cycle: a short cycle (present at fast heart rates) will be associated with a short refractory period, and a long cycle (present at slow heart rates) will be associated with a long refractory period.

These facts help explain some of the observed features of wide QRS tachycardias.

1. As there is inhomogeneity of refractory periods within the conducting system, impulses entering the conducting system from normal supraventricular sources may encounter refractory areas within the normal conduction system when the heart rate is fast. This will be manifested as aberrancy in the QRS complex. The slower inhomogeneous impulse conduction through the ventricle results in a widened QRS complex.
2. If the aberrancy of conduction occurs in a normal conducting system secondary to an increase in refractoriness, it is much more likely to occur within the right than the left ventricular conduction system. This would result in a wide QRS with a right bundle branch block pattern. However, the left bundle may be affected as well (Fig. 1*A* and *B*).
3. If the heart rate is constantly changing (such as in atrial fibrillation), a slow heart rate (long cycle) followed by a rapid heart rate (short cycle) will find the connecting system refractory to the action potential impulse. This will be manifested as a wide, aberrantly conducted QRS complex, the nature of which will depend on the state of refractoriness of the various parts of the conduction system.
4. Anything that interferes with the integrity of the conduction system will change the nature and normal progression of conduction and therefore the QRS will be widened in configuration. Factors that can influence conduction in this manner include intrinsic cardiac disease, drug effects, and electrolyte abnormalities.
5. The point of origin of the impulse will determine the route of spread, which conducting fibers will be involved, and in what order. This will alter the QRS shape and may prolong its duration. This is an important concept for understanding QRS abnormalities seen in patients with ventricular pacemakers, accessory bundles, and ventricular ectopy.

With this as a background, we can begin to approach the wide QRS complex tachycardias in an organized fashion.

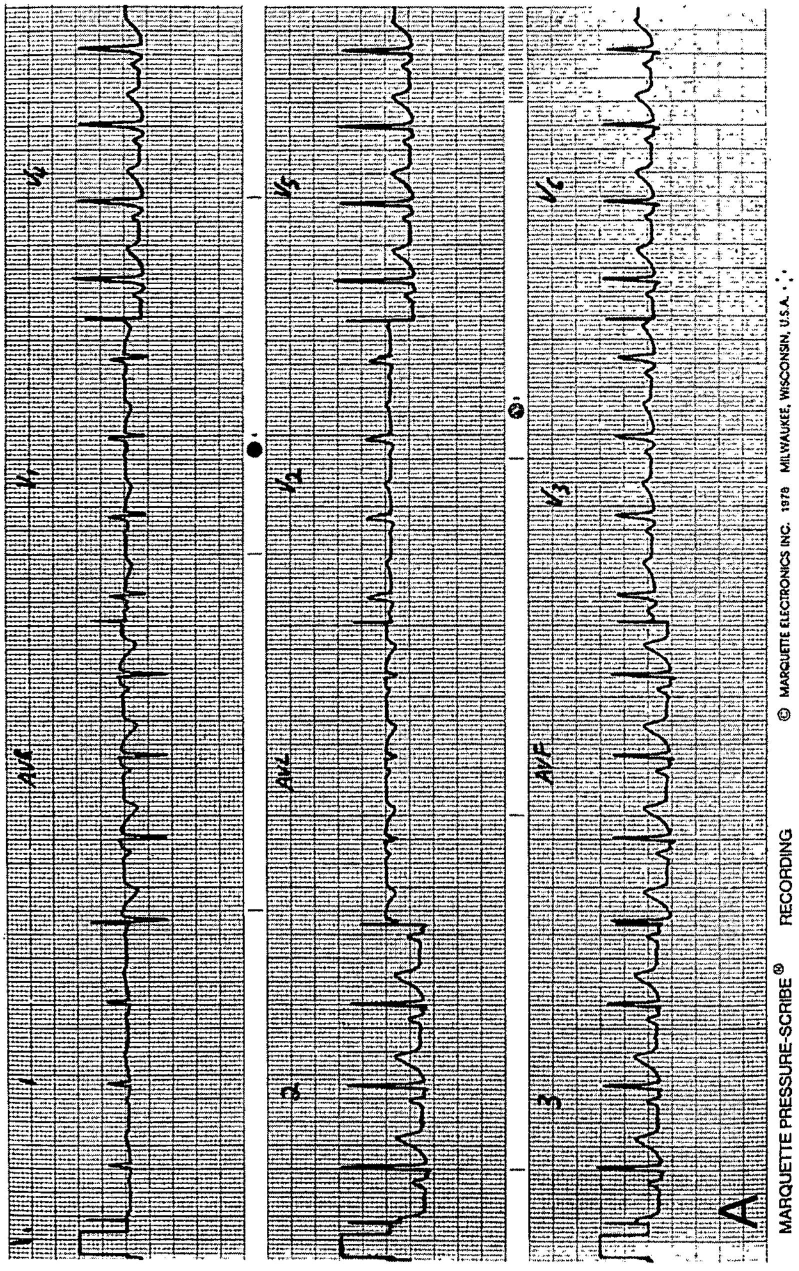
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Figure 1. (A) Normal ECG with heart rate of 80. *Figure continued on next page.*

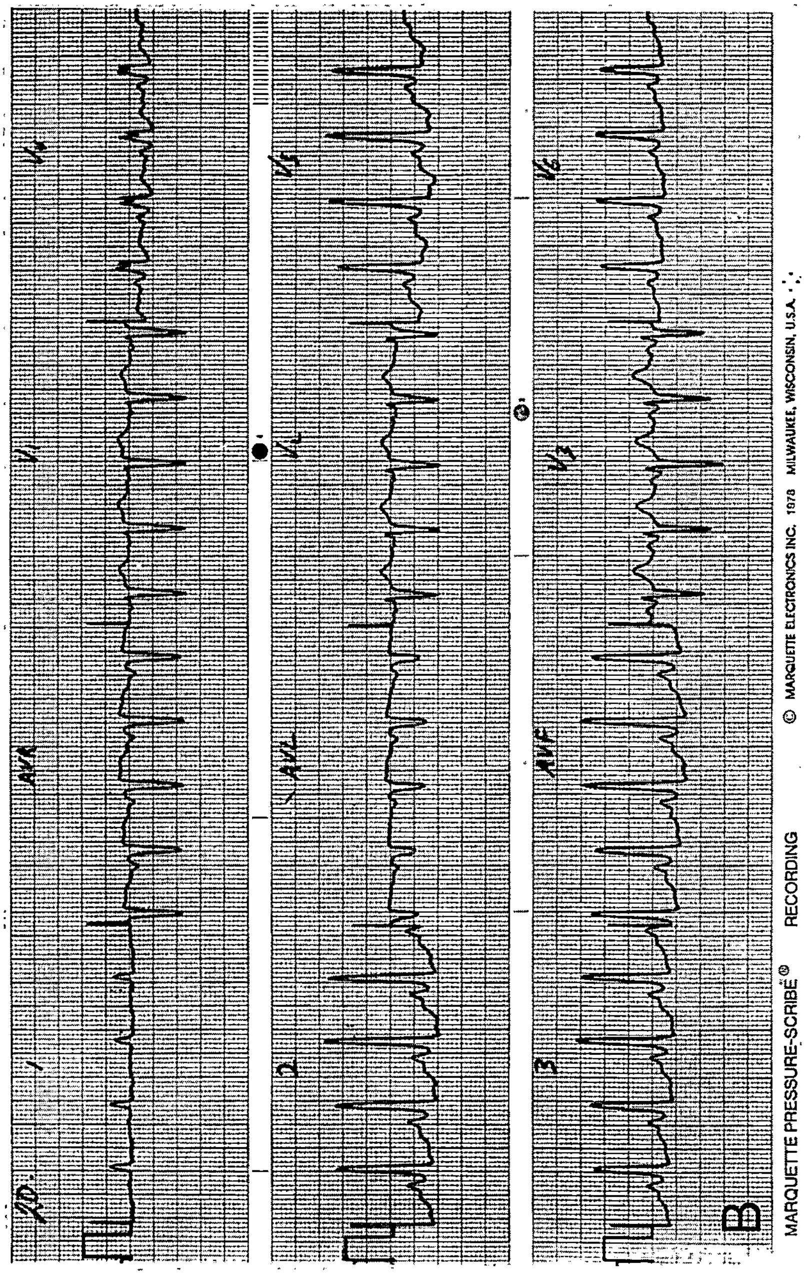
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Figure 1 (*Continued*). (*B*) Note development of a left bundle branch block (QRS duration > 0.12 seconds, predominantly negative QRS deflection in V, and positive deflection in V_6) when heart rate increases to 110.

SUPRAVENTRICULAR TACHYCARDIAS WITH PRE-EXISTENT BUNDLE BRANCH BLOCK

Pre-existing bundle branch block patterns on the ECG are not infrequent in the adult population. The presence of a right or left bundle branch block pattern on the ECG can usually be easily differentiated from the normal QRS by the duration of the QRS complex. With either type of bundle branch block pattern, the QRS duration will be greater than 0.12 seconds (three small boxes on a standard ECG). Determining whether the patient has a right or left bundle branch block can also be readily accomplished by examining lead V_1. If the wide QRS complex is predominantly upright, it is a right bundle branch block pattern. With a left bundle branch block pattern, the QRS complex will be predominantly downward in this lead. In lead V_6, a right bundle branch pattern will have a predominantly downward deflection of the QRS complex and a left bundle branch pattern will have a predominantly upright deflection of the wide QRS complex (Figs. 1 and 2).

When the patient with a pre-existing bundle branch block develops a supraventricular tachycardia (SVT), differentiation from ventricular tachycardia (VT) may be difficult. Because all conducted impulses from above the ventricle would most likely be conducted through the remaining intact ventricular pathways, the QRS complex will usually have an identical morphology and duration to those seen during normal sinus rhythm.[3] If the QRS complex has a different morphology, it is likely to be of ventricular origin. Rarely, however, a ventricular tachycardia may have the same QRS morphology as a sinus beat in a single lead. Evaluating other leads can quickly aid in differentiation. Another valuable point distinguishing supraventricular from ventricular tachycardia in patients with pre-existent bundle branch block, is the duration of the QRS. If the QRS duration increases during the episode of tachycardia, it is probably ventricular in origin and should be treated as such.

SUPRAVENTRICULAR TACHYCARDIA WITH ABERRANT CONDUCTION

A new wide complex QRS resulting from a supraventricular impulse is not an indication of ventricular conduction system pathology per se; it may merely be an extension of the intrinsic inhomogeneity of conduction within the ventricle. The etiology of the accelerated supraventricular rate of depolarization may be pathologic in origin, but it may also be an appropriate response to a physiologic stress. The site of entry of the supraventricular impulse to the ventricular conduction system can be in the normal conduction pathway through the AV node and down the His bundles or via bypass tracts such as the direct atrial-ventricular conduction pathway present in patients with Wolff-Parkinson-White syndrome (Fig. 3). Wide complex QRS pat-

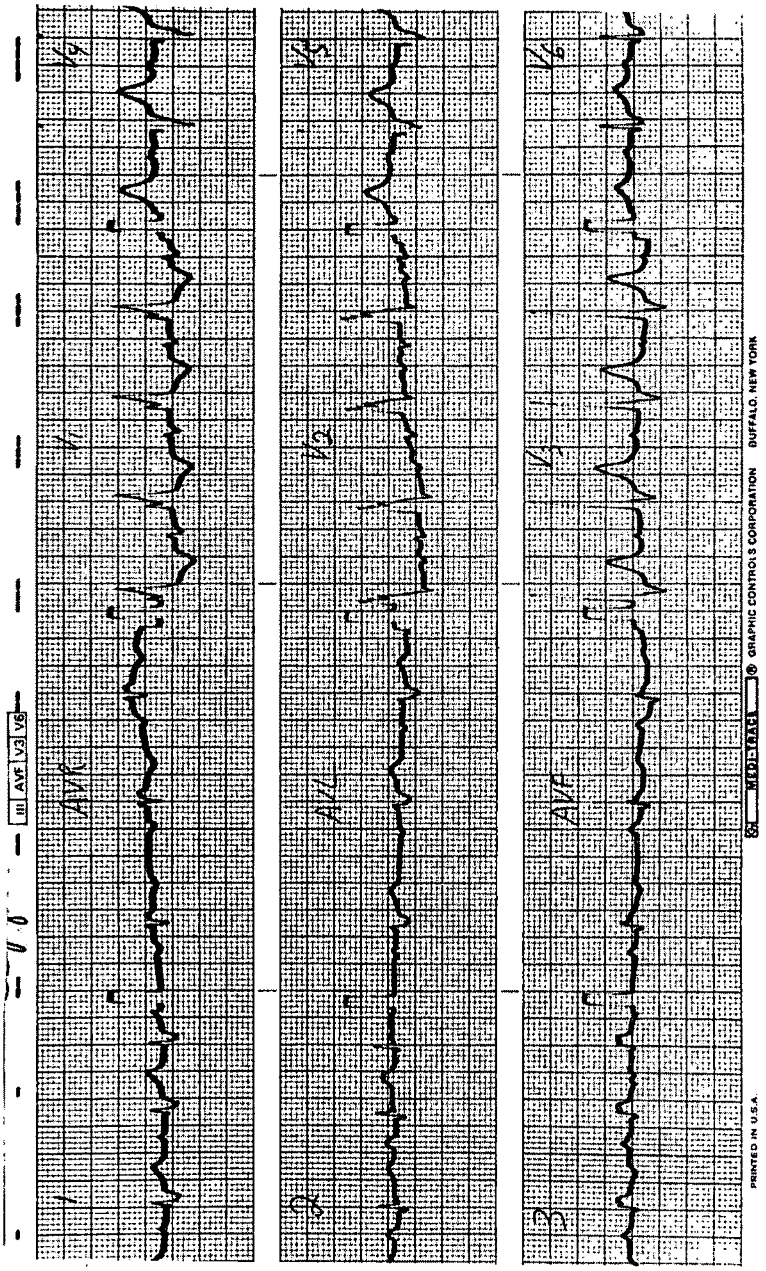

Figure 2. Right bundle branch block. Note wide S wave in I and RSR′ pattern in V_1 and V_2.

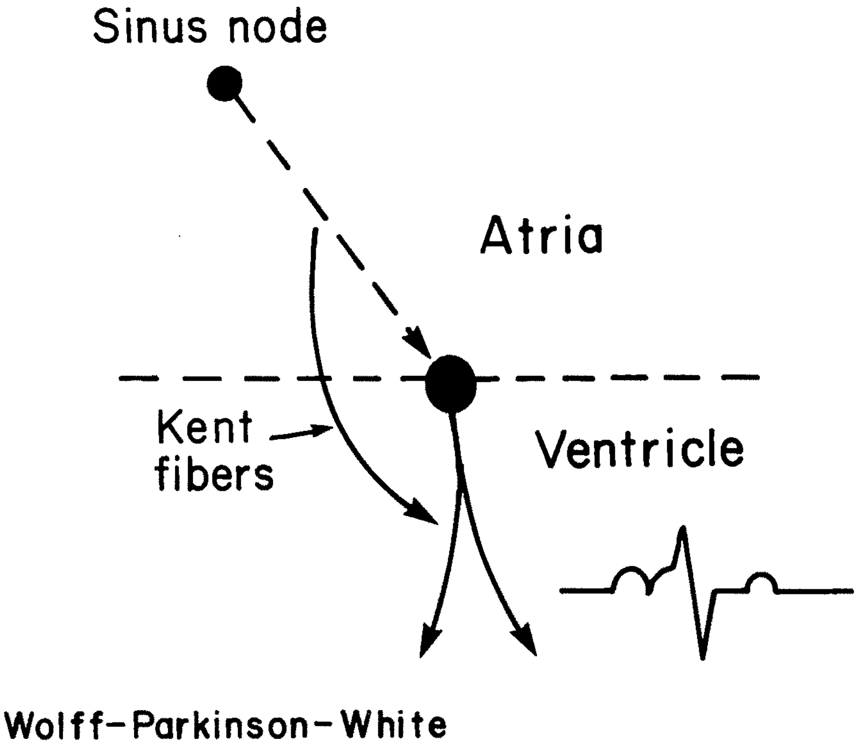

Figure 3. Accessory pathway through Kent fibers in the Wolff-Parkinson-White syndrome. Conduction through this pathway results in a wide QRS complex, a short PR interval, and a delta wave.

terns that follow the normal conduction pathway result from rate-related aberrancy of conduction. Those that are present in patients with bypass tracts, result from *fusion* of two depolarizations. The first proceeds down an accessory pathway producing an abnormal sequence of depolarization; the second is normal conduction with delay through the AV node. The result of this "summation" of an abnormal, wide QRS with a normal QRS is a QRS different in morphology and duration from the normal QRS.

Aberrancy of conduction results when a supraventricular impulse arrives at the ventricular conduction system when it is still partially refractory. This can be seen with atrial fibrillation, atrial flutter, atrial premature contractions (which can initiate an atrial tachycardia), reentry tachycardias, and rate-related bundle branch block seen with sinus tachycardia.

The electrocardiographic distinction between SVT with aberrant conduction and VT may be extremely difficult at times because features of both arrhythmias overlap.[18] Under certain circumstances an SVT may have all the electrocardiographic features associated with

Table 2. *Differentiation of Supraventricular Tachycardia with Aberrant Conduction from Ventricular Tachycardia*

	SVT	VT
Evidence of AV dissociation	No	Yes
QRS greater than 0.14 seconds	No	Yes
Marked left axis deviation	No	Yes

VT and therefore can only be distinguished with more invasive electrophysiologic studies.

Numerous electrocardiographic criteria have been proposed to help differentiate between a supraventricular or ventricular origin of a wide QRS tachycardia.[5, 15–17] The most reliable criterion to determine the origin of a wide QRS tachycardia is the presence of AV dissociation, which identifies the arrhythmia as ventricular (Table 2).[17] Unfortunately, AV dissociation cannot be identified on the ECG in over 25 per cent of patients with VT. The presence of a fusion beat or actual intermittent antegrade capture of the ventricle by an atrial beat during a wide QRS tachycardia is diagnostic of VT, but this occurs infrequently.

Findings on physical examination suggestive of AV dissociation such as cannon waves in the neck, changing amplitude of the first heart sound, and varying systolic blood pressure on successive beats, should be noted. Their presence strongly supports a diagnosis of VT. The absence of AV dissociation does not exclude the diagnosis of VT, because 1:1 retrograde ventricular-atrial conduction occurs in some patients with VT and in these patients AV dissociation will not be present.

The width of the QRS complex is a second criterion that is useful for evaluating the type of wide QRS tachycardia that is present. In the absence of pre-existent bundle branch block or pharmacologic therapy known to influence QRS duration, a QRS width of greater than 0.14 seconds is highly suggestive of a ventricular origin of the tachycardia and a QRS width of less than 0.14 seconds strongly favors the diagnosis of SVT with aberrancy. In the study by Wellens and associates,[17] all patients with aberrant conduction had a QRS width of less than 0.14 seconds. Seventy per cent of the episodes of VT had a QRS width of greater than 0.14 seconds.

The third criterion is the presence of an extreme left axis deviation, which suggests a ventricular origin of the tachycardia. Although other criteria (such as the shape of the QRS complex) have been reported, they have not been as well accepted because they are not specific enough to distinguish SVT from VT.

When the anesthesiologist is confronted with a patient who suddenly develops a wide QRS tachycardia, a sense of urgency often precludes obtaining a 12-lead ECG or taking the time necessary to look for the distinguishing features discussed previously. In this situation certain clinical findings are very useful for diagnosing the type of arrhythmia present. If the patient has a history of myocardial infarction and has never had tachycardias prior to the infarction, it is likely that the wide QRS tachycardia is VT.[14] If the patient has a long history of tachycardia, has no known organic heart disease, or has ventricular pre-excitation during sinus rhythm, it is likely that the wide QRS tachycardia is supraventricular in origin.

If the exact diagnosis remains unclear despite the history, physical evaluation, and electrocardiographic evaluation, then one should assume that the arrhythmia is VT.

PRE-EXCITATION SYNDROMES

In patients with accessory AV pathways, a variety of arrhythmias may result in wide QRS tachycardias. Paroxysmal tachycardias have been estimated to occur in 50 to 80 per cent of patients with pre-excitation. Seventy-five per cent are re-entrant tachycardias, 20 to 25 per cent are atrial fibrillation. Atrial flutter and VT occur rarely.[2, 12]

Recognition of the presence of an accessory pathway in a tachycardic patient is important because these wide QRS tachycardias are easily mistaken for VT. In the pre-excitation syndromes the QRS may be normal or prolonged while the PR interval is shortened. The 12-lead ECG is the primary modality for diagnosing the presence of a pre-excitation syndrome. Wolff-Parkinson-White syndrome is the most common of several pre-excitation syndromes with a reported incidence of 1 to 3 per 1000 population. The combination of a delta wave following a shortened PR interval is characteristic of Wolff-Parkinson-White syndrome. The delta wave may be present intermittently and the diagnosis of Wolff-Parkinson-White syndrome may first be made in the perioperative period when physiologic stresses alter the refractory period of the AV node[7] (Fig. 4).

When pre-excitation occurs in a patient with Wolff-Parkinson-White syndrome, the atrial depolarization spreads simultaneously down the accessory pathway and through the normal conduction pathway. In relation to atrial events, part or all of the ventricle is activated earlier by this atrial impulse than would be expected if the impulse activated the ventricle by way of the normal AV node and His Purkinje system. The delta wave represents areas of the ventricle that are depolarized by electrical input carried through the accessory pathway. The resulting QRS ventricular complex is therefore a fusion of the atrial impulse activating ventricular myocardium over the accessory and normal conduction pathways.

In Wolff-Parkinson-White syndrome the most common accessory pathway runs from the atrium to the Purkinje fibers. The two competing routes of AV conduction have different speeds of depolarization, conduction velocities, and effective refractory periods. These electrophysiologic differences predispose these patients to the development of re-entrant tachyarrhythmias.

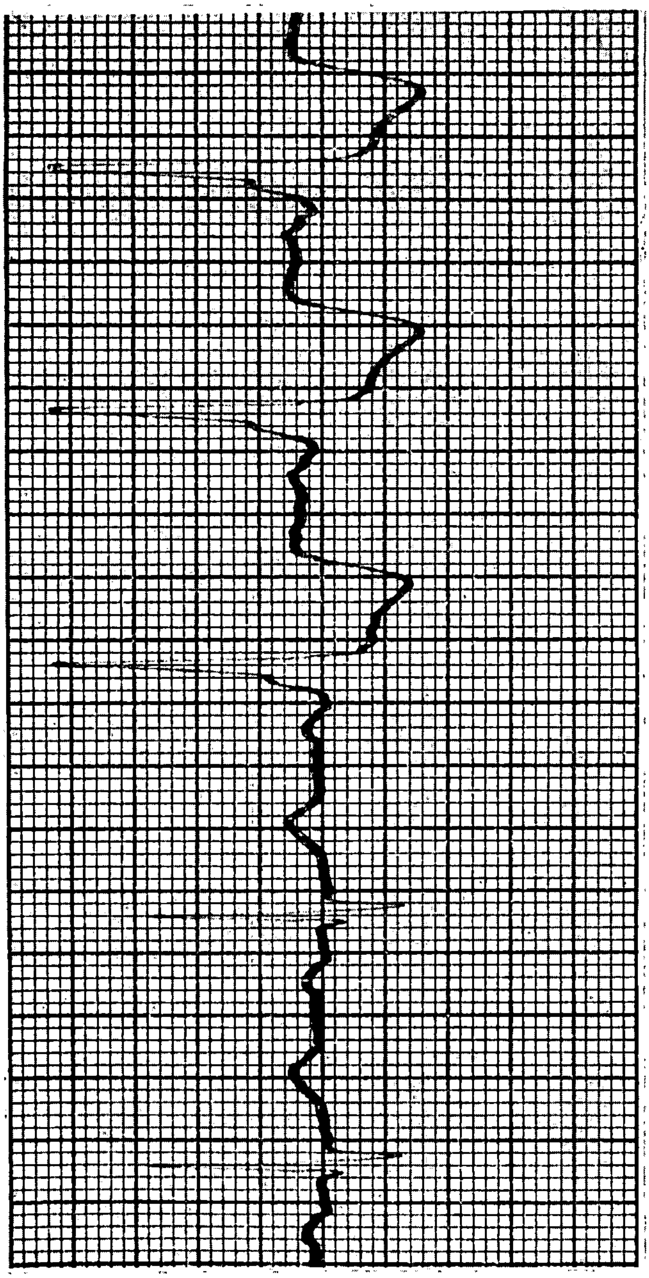

Figure 4. Intermittent conduction through an accessory pathway results in the onset of a delta wave and a wide QRS complex in the third to fifth complexes.

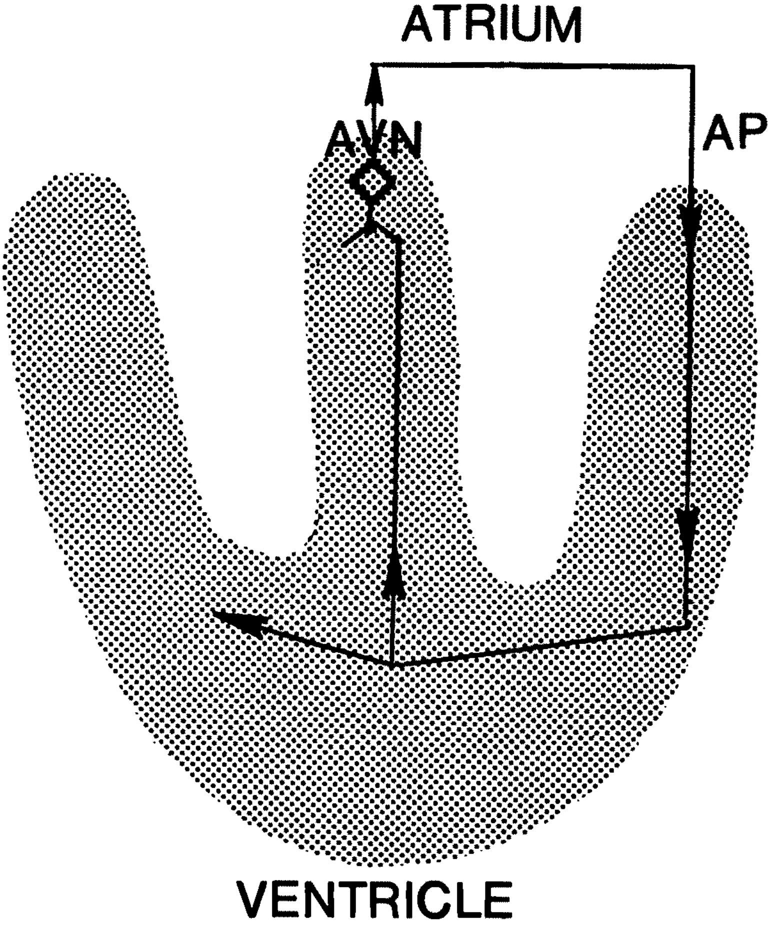

Figure 5. Orthodromic reciprocating tachycardia results when the impulse is conducted in an antegrade fashion over the normal conduction pathway and re-enters the atrium retrograde through an accessory pathway.

Because the accessory tract usually has a longer refractory period than the normal pathway, a premature atrial contraction may be conducted in an antegrade fashion to the ventricle over the normal conduction pathway blockade. After the ventricle is depolarized, the impulse re-enters the now receptive Purkinje-atrial pathway retrograde, producing a reciprocating tachycardia (orthodromic reciprocating tachycardia) (Fig. 5). This is the most frequent arrhythmia seen in patients with accessory AV pathways.[11] This arrhythmia usually produces a regular atrial tachycardia with a narrow QRS complex. However, a wide QRS tachycardia will result in patients with either a preexistent bundle branch block or a rate-related (functional) bundle branch block. The presence of a functional bundle branch block is a

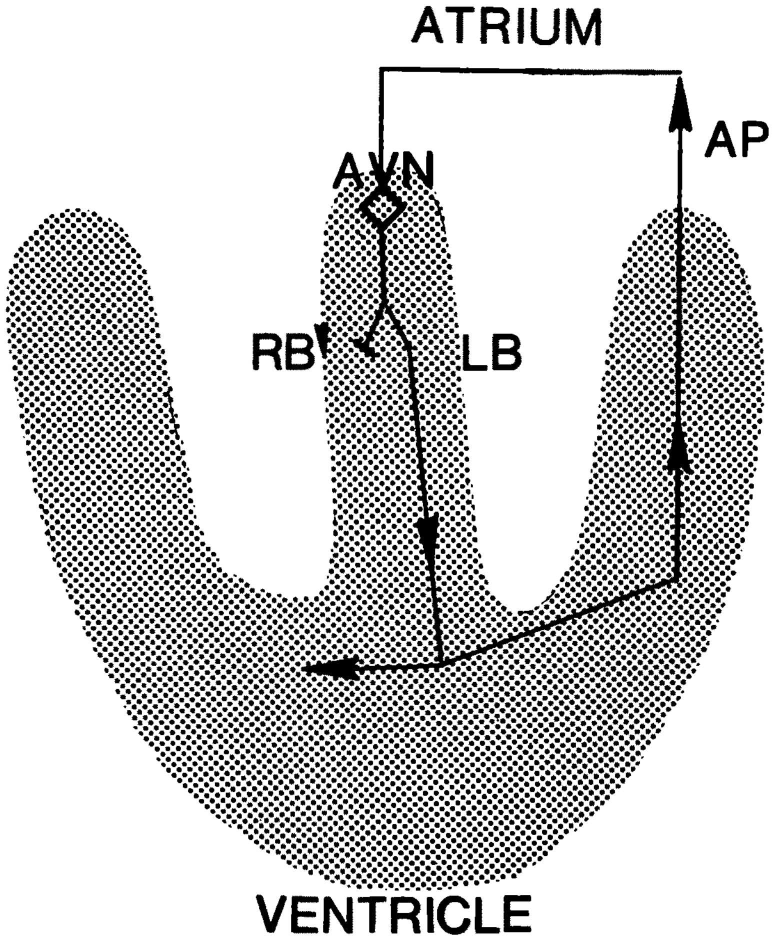

Figure 6. An antidromic reciprocating tachycardia results when the impulse is conducted in an antegrade fashion over the accessory pathway and then re-enters the atrium retrograde through the Purkinje-His-AV node system.

common mechanism for a wide QRS tachycardia in patients with an accessory pathway.

In the unusual circumstance where the bypass tract is of shorter refractoriness, the atrial impulse will move down the accessory pathway and produce a wide QRS complex with a delta wave. A premature atrial contraction may initiate an antidromic reciprocating tachycardia in which antegrade conduction from the atrium to the ventricle takes place by way of an accessory pathway while retrograde ventricular-atrial conduction occurs over the Purkinje-His-AV node system (Fig. 6). Antidromic reciprocating tachycardia should be suspected as the etiology of a wide QRS tachycardia when the QRS complex during the tachycardia has a similar morphology to the pre-excited QRS complex present during sinus rhythm on an ECG.

In both orthodromic and antidromic reciprocating tachycardias, the presence of an accessory pathway is essential for the development of the tachycardia. Patients with an accessory pathway may develop SVTs in which the accessory pathway is not essential for the development of the arrhythmia but its presence could result in the production of a wide QRS tachycardia.

If an SVT develops (atrial fibrillation, atrial flutter, paroxysmal atrial tachycardia), dangerously high ventricular rates may be present if conduction occurs antegrade through the accessory pathway. Impulses will be conducted 1 to 1 to the ventricle because the AV node, with its intrinsic delay, is bypassed. The resulting wide complex tachycardia will mimick VT (Fig. 7). When the ventricular response is greater than 200 beats per minute, cardiac output may be significantly decreased and myocardial ischemia may result. There is a risk that when a patient with Wolff-Parkinson-White syndrome develops a supraventricular arrhythmia with an extremely rapid ventricular response, the arrhythmia may degenerate into VT or VF.

The differentiation of VT from SVT with a wide QRS complex owing to a pre-excitation syndrome may be difficult. Close evaluation of a long rhythm strip will often permit identification of atrial fibrillation as the basis of an irregular ventricular rhythm. In addition, obvious alteration in the QRS configuration may be seen that is suggestive of a variable degree of ventricular pre-excitation.

When a relatively regular wide QRS tachycardia is present and identification of the type of arrhythmia is uncertain, carotid sinus massage may be helpful. If the arrhythmia is of supraventricular origin, it may respond by resumption of sinus rhythm. In some patients only electrophysiologic studies will definitely be able to diagnose the type of arrhythmia present. Obviously, this is of little value to the anesthesiologist in the operating room or recovery room, so if the diagnosis remains uncertain but VT is a possibility, the patient should be treated as if they have VT.

VT is an additional etiology of a wide QRS tachycardia in patients with Wolff-Parkinson-White syndrome. It may arise from an ectopic ventricular focus or from re-entry within the ventricle.

VENTRICULAR TACHYCARDIA

The wide QRS tachycardias of supraventricular origin are occasionally associated with reduced cardiac output. Conversely, VTs are usually associated with a marked decrease in cardiac output; ventricular fibrillation has no cardiac output at all. Ventricular arrhythmias have a widened QRS complex, the morphology of which depends on the site of origin of the beat. In general, the closer the origin is to the interventricular septum and conducting fibers, the less the QRS will be deformed. Impulses arising in various fascicles will produce a char-

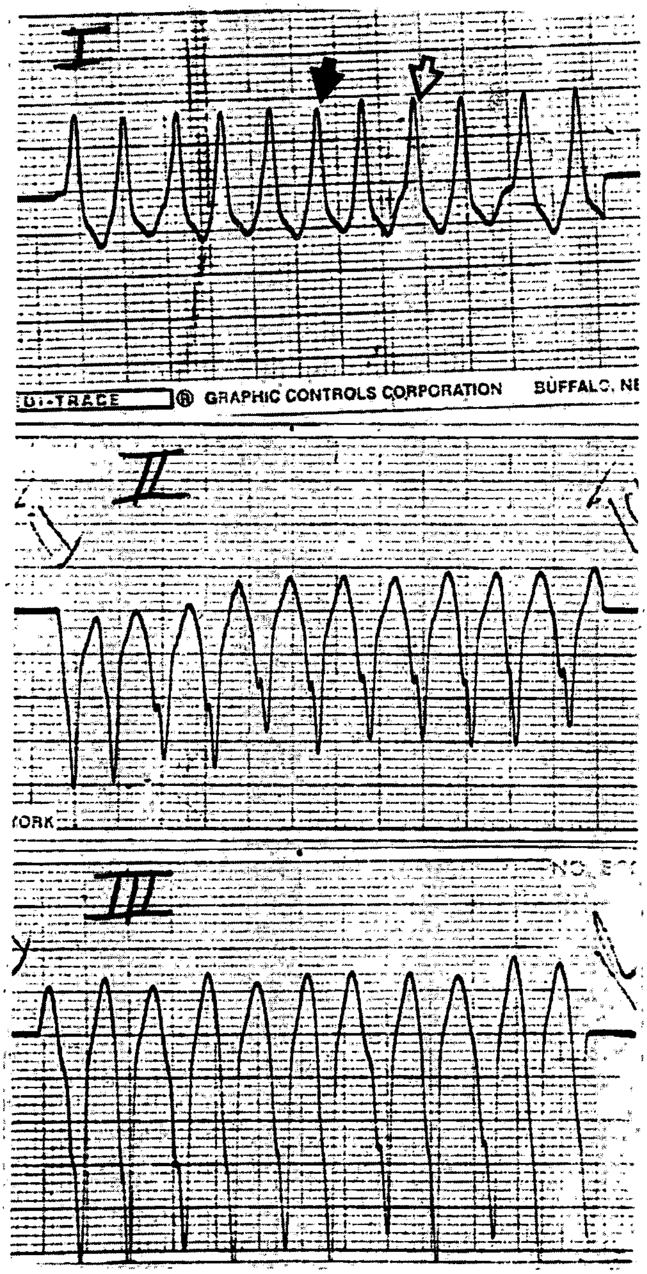

Figure 7. Rapid atrial fibrillation in a patient with the Wolff-Parkinson-White syndrome. Note the varying RR interval and the varying width of the QRS complex (*closed and open arrows*).

acteristic pattern; the region they originate from will be depolarized first followed by the remaining ventricular myocardium. A left anterior bundle ectopic depolarization will have a pattern similar to a right bundle branch block with left posterior hemiblock. When the ectopic impulse arises from the right ventricle, the right side of the myocardium and conduction system will be depolarized first, followed by the left. When contrasted with the normal progression of depolarization, it will appear as though the left bundle is slower or "blocked" as compared with the right, resulting in a left bundle branch block pattern. When a patient has a functioning transvenous ventricular pacemaker in place, when the pacemaker fires, a wide complex QRS will be seen. Because the pacemaker lead stimulates the right ventricle first, the resulting wide QRS complex will have a left bundle branch pattern.

Another morphologic feature associated with a ventricular ectopic complex is that the ST segment usually goes in a direction opposite to that of the terminal portion of the QRS complex.

An isolated QRS complex of ventricular origin is termed a premature ventricular contraction if the complex is premature, or a ventricular escape beat if no other primary pacemaker is firing. When three or more premature ventricular contractions occur in succession at a rate greater than 100 per minute (usually between 140 and 200), it is termed VT (Fig. 8). When these ventricular beats occur at a rate slower than 100 per minute an idioventricular rhythm is present.

VT can be precipitated by supraventricular, ventricular, or exogenous stimuli such as micro or macro shocks. Stimulation of the ventricle during the vulnerable period (approximated on the surface ECG by the T wave) can initiate VT; however, most episodes arise from premature ventricular contractions that occur at times other than the vulnerable period. VT is usually seen in patients with severe myocardial disease (ischemic, rheumatic, myopathic). It occasionally develops in patients with mitral valve prolapse.

VT is always considered to be clinically significant because: (1) Cardiac output may be markedly reduced, (2) the arrhythmia may degenerate into ventricular fibrillation, and (3) it serves as a marker for the possible presence of severe myocardial disease.

The diagnosis of VT should be strongly considered when a series of three or more bizarrely shaped premature ventricular contractions occur that have a duration exceeding 120 msec with the ST-T vector pointing opposite to the major QRS deflection. The RR interval, although usually exceedingly regular, may vary. Therefore, the regularity of the arrhythmia is not completely reliable in differentiating between SVT and VT. However, markedly irregular RR intervals indicate the presence of atrial fibrillation with left or right bundle branch block, with aberrant ventricular conduction, or with conduction through an accessory pathway rather than VT.

Atrial activity during episodes of VT is usually independent of ventricular activity (AV dissociation). Less commonly, retrograde activation of the atria occurs. Occasionally, in the presence of AV dis-

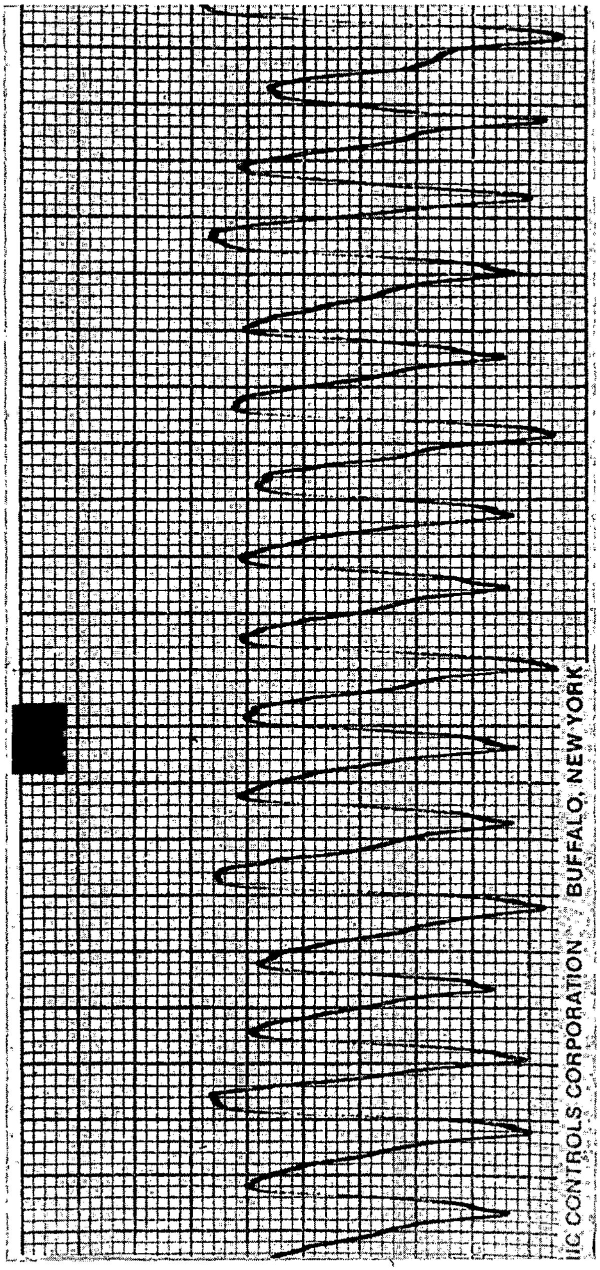

Figure 8. Ventricular tachycardia.

sociation, an atrial beat may conduct through the AV node and depolarize the ventricle resulting in a normal-appearing complex. This finding in a patient with a wide QRS tachycardia supports the diagnosis of VT. The appearance of a fusion beat on the ECG tracing also supports the diagnosis of VT.

Evaluation of the neck veins or central venous pressure trace may help make a diagnosis of VT in patients with wide QRS tachycardia. The presence of large A waves (cannon waves) suggests that AV dissociation is present and therefore supports a diagnosis of VT.

Several unusual varieties of VT have been described. These include the following.

1. Repetitive VT: These are runs of VT separated by 1 to 2 sinus beats. It is relatively benign and can occur in the absence of severe underlying cardiac disease.
2. Polymorphous VT: Many different QRS shapes are manifested. The presence of this pattern implies severe underlying cardiac disease.
3. Bidirectional/alternating: Here the direction of the QRS complex changes alternately or periodically. This variant is almost always due to digitalis intoxication.
4. Torsade de pointes (twisting of the points)[1, 6, 9] (Fig. 9): This is a form of paroxysmal VT that meets the following morphologic criteria: (1) a ventricular rate typically greater than 200 per minute; (2) QRS morphology that displays alternating polarity in an undulating pattern so that complexes appear to be twisting about the baseline; and (3) the arrhythmia is typically nonsustained and may be a variety of polymorphous VT.

The mechanism underlying the development of torsade de pointes is not well understood. Because this arrhythmia occasionally degenerates into ventricular fibrillation, it may represent a transitional form of arrhythmia between conventional monoform VT and ventricular fibrillation.

Torsade de pointes usually occurs in a clinical setting in which a specific well-recognized predisposing cause can be identified. It usually is associated with either an acquired or congenitally prolonged QT interval.[4, 9] Acquired prolongation of the QT interval may be seen in patients receiving drugs such as quinidine and procainamide. It also may develop following right radical neck surgery.[10] Recognition of this variety of VT is essential because its treatment (isoproterenol infusion or placement of a temporary transvenous pacemaker for overdrive pacing) differs from treatment of other forms of VT. In addition, if untreated it may evolve into ventricular fibrillation.

Although the characteristic electrocardiographic pattern (see Fig. 9) usually helps to differentiate this arrhythmia from other forms of VT, if only a single ECG lead is being evaluated, the morphology may appear uniform and thus difficult to differentiate from others.

VENTRICULAR FIBRILLATION

Ventricular fibrillation also has wide, very bizarre, and often changing QRS patterns. The QRS complex is extremely disorganized

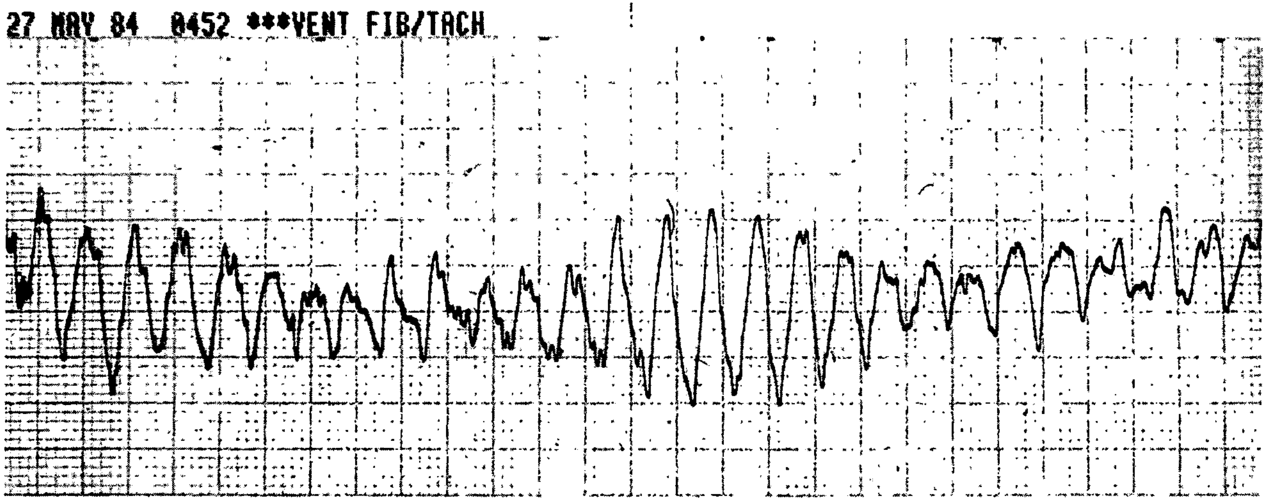

Figure 9. Torsade de pointes. Note characteristic undulating pattern. (See text for full description.)

in comparison to any of the previously mentioned arrhythmias. In addition to its unmistakable ECG appearance, this arrhythmia is not associated with any forward blood flow and once artifact has been excluded, advanced cardiac life support must be initiated and the patient should be immediately defibrillated.

CLINICAL SCENARIOS

Sinus tachycardia differs from the other SVTs in that its onset is usually gradual whereas all the others have an abrupt onset. Atrial and nodal tachycardias are abrupt in onset. Atrial tachycardias have an abnormal P wave. The P wave of nodal tachycardia may not be seen on the ECG or may appear after the QRS complex (retrograde conduction). These tachyarrhythmias can be precipitated by a sudden ectopic atrial or nodal impulse. The same stresses that induce a sinus tachycardia can produce atrial and nodal tachycardias. In addition, alcohol, tobacco use, digitalis toxicity, chronic lung disease, and bypass tracts of the pre-excitation syndromes are predisposing factors.

Atrial fibrillation usually occurs in patients with a pathologically enlarged left atrium from such diseases as rheumatic heart disease, nonrheumatic valvular heart disease, hypertensive cardiovascular disease, and atrial septal defect. It is seen as well in patients with sick sinus syndrome, ischemic heart disease, advanced lung disease, acute hypoxemia, hypercarbia, thyrotoxicosis, and pulmonary embolism. In normal patients it can follow binge drinking, exercise, emotional stress, and surgery.

Atrial flutter is seen almost exclusively in patients with organic heart disease. It occasionally develops in patients with acute respiratory failure and pericarditis.

VTs are frequently associated with organic heart disease, usually ischemic in nature, as well as nonischemic cardiomyopathies, prolonged QT syndromes (congenital and acquired, such as post right radical neck dissection), drug toxicity (for example, digitalis, quinidine), and electrolyte imbalance (hypokalemia, hypomagnesemia, or hypermagnesemia). Prolongation of the QT interval can result in the development of torsades de pointes. This is especially important to recognize, as discontinuation of drugs that prolong the QT interval often leads to resolution of the arrhythmia. Drugs that are often used for chronic treatment of ventricular arrhythmias (quinidine and procainamide) should be avoided in these patients as they can result in further prolongation of the QT interval and will not successfully treat the torsades de pointes.

TREATMENT

Supraventricular Tachycardia with Aberrancy

The goal is to slow down the rate of impulses bombarding the ventricular conduction system. This may be accomplished by either slowing down the rate of the supraventricular focus or impeding passage of the impulses across the AV node. Drugs such as the beta-blockers, calcium channel blockers, and digitalis would be appropriate.

Pre-excitation Syndrome with Wide QRS

The goals of therapy are to increase bypass tract refractoriness, increase conduction down the normal pathways, and limit the number of atrial and ventricular premature contractions that may precipitate the re-entrant tachycardias. The drugs of choice in patients with Wolff-Parkinson-White syndrome and recurrent tachyarrhythmias are procainamide and lidocaine. Beta-blockers, calcium channel blockers, and digitalis should be avoided as they can shorten the refractory period of the accessory tract and thereby may dangerously increase the ventricular rate.

Ventricular Tachycardia

Cardioversion is used for the unstable patient. For the stable patient lidocaine can be given rapidly as a bolus followed by a continuous infusion and has less cardiovascular side effects than other effective antiarrhythmic agents. Procainamide has the advantage of helping differentiate supraventricular from ventricular tachycardias as well as suppressing ventricular tachycardia extremely well. However, it cannot be given rapidly intravenously (hypotension may be precipitated). Other useful drugs include bretylium, quinidine, and disopyramide.

Treatment of the special case of torsade de pointes depends on what is causing the prolonged QT interval. If it is congenital in origin, excess catecholamine secretion is a common precipitating cause for the VT. In this situation beta-blockade is indicated. Other drugs that can be used are phenytoin, bretylium, and verapamil. A left stellate ganglion block may also be helpful. For treatment of torsades de pointes associated with an acquired prolonged QT interval, discontinuation of the responsible drug along with attempts to shorten the QT interval by increasing the heart rate with ventricular pacing or isoproterenol infusion, are indicated.

When dealing with any of these arrhythmias, detection and correction of electrolyte abnormalities, hypoxemia and hypercarbia, and ischemia should be high on the list of priorities. These are frequent etiologies of these arrhythmias and are often easily corrected.

TREATMENT OF WIDE QRS TACHYCARDIAS

To determine if immediate treatment is necessary, the impact of the arrhythmia on the patient's hemodynamic status needs to be assessed. This involves immediate evaluation of the circulation (blood pressure and pulse), respirations, and mental status (if the patient is not under general anesthesia). In addition, if indwelling monitors such as an intra-arterial catheter or pulmonary artery catheter are in place, the impact of the arrhythmia on stroke volume can be visually examined. The urgency of the response is dictated by the degree of hemodynamic impairment and the perceived threat to the patient's well being. If the patient is unable to maintain an adequate cardiac output as demonstrated by the presence of significant hypotension, altered mental status, chest pain, or if there is a deterioration in respiratory status (decreased rate or apnea), or if wave forms on the arterial or pulmonary artery trace disappear with the given rhythm, then electrical cardioversion should be immediately instituted, as most supraventricular and ventricular arrhythmias respond to this therapy.

If the patient appears to have adequate perfusion with the arrhythmia, then clues from the patient's history, physical examination, prior and current 12-lead ECGs, and laboratory data can be examined to delineate the precise nature of the arrhythmia and to guide selection of appropriate therapy.

SUMMARY

Although evaluation of the patient with a wide QRS tachycardia may be difficult, an organized systematic approach to interpreting the ECG along with review of the patient's history and physical findings usually permits the physician to make a correct diagnosis. Failure to follow this approach may lead to a therapeutic misadventure with increased patient morbidity.

The differential diagnosis of a wide QRS tachycardia includes sinus tachycardia with either pre-existing or rate-related bundle branch block, SVT with aberrant conduction, pre-excitation syndromes, VT, and ventricular fibrillation. Electrocardiographic and clinical clues will allow the anesthesiologist to distinguish between these arrhythmias in most instances.

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Recognition and Treatment of Bradycardias and Atrioventricular Block

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Bradycardias and conduction abnormalities are occasionally encountered by the anesthesiologist. Concerns arise regarding stability of the rhythm, response to pharmacologic agents, and the possible need for temporary electrical pacing. A knowledge of the site of the arrhythmia, its physiology and natural history help answer these questions. In general, conduction disturbances high in the system (such as the atrioventricular [AV] node) are benign because they do not progress to more severe blockade, they respond to pharmacologic agents such as atropine and isoproterenol, and the subsidiary pacemakers are fast enough to maintain hemodynamic stability. Disturbances lower in the system are more pathologic and may result in hemodynamic instability.

SINUS RHYTHM

Although special techniques can record the electrical activity of the sinus node,[37, 78] generally its activity is inferred by atrial depolarization, which is visible as the P wave on the surface electrocardiogram. The crescent-shaped sinus node is located superficially at the junction of the superior vena cava and the right atrium. Thus, if the sinus node is the pacemaker, the atrial depolarization (P wave) vector should point downward, anteriorly, and to the left. The P wave on the electrocardiogram (ECG) should be upright in leads I, II, and aVF. Inverted P waves in these leads suggest a nonsinus pacemaker.

The blood supply to the sinus node consists of a single sinus node artery that originates from the right coronary artery in 55 per cent of

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patients and from the left circumflex artery in 45 per percent of patients.[42, 43] A patient with significant coronary atherosclerosis of these vessels may have bradycardia due to decreased perfusion of the sinus node; however, this is not common.

Both sympathetic and parasympathetic nerves modify the activity of the sinus node.[45] Vagal stimulation slows the sinus rhythm by decreasing the slope of phase 4 depolarization. Sympathetic stimulation speeds the sinus rhythm by increasing the slope of phase 4 depolarization. The autonomic nervous system allows for precise adjustments in heart rate for diverse conditions such as sleep and exercise. The variation in sinus rate with respiration (sinus arrhythmia)[12] is also due to autonomic effects (Fig. 1). These autonomic influences are conspicuously absent in patients who have received a cardiac transplant.[50]

Excessive parasympathetic stimulation can cause sinus bradycardia. For example, in carotid sinus hypersensitivity,[40, 104] even a mild stimulus such as a tight shirt collar can cause a marked bradycardia. Vasovagal bradycardia can also occur from various states such as fear, pain, and nausea. In addition, receptors in the left ventricle have been described that respond to pressure or ischemia by stimulating a parasympathetically mediated bradycardia (Bezold-Jarish reflex) in exercizing patients with aortic stenosis[58] and in patients with inferior myocardial infarctions.[59]

SICK SINUS SYNDROME

In 1954 Short[91] reported a clinical syndrome of sinus node dysfunction that involved periods of tachycardia and bradycardia. Ferrer[29] described its characteristics as persistent sinus bradycardia, sinus arrest with escape rhythms, sinus arrest without subsidiary escape rhythm, atrial fibrillation with slow ventricular response, inability of the heart to resume sinus rhythm following cardioversion of atrial fibrillation, and episodes of sinoatrial exit block (see Fig. 1). The syndrome is not a necessary consequence of aging since sinus arrest and severe bradycardia are not common in active elderly patients.[16] In fact, sick sinus syndrome has been described in adolescents.[8, 48] Although various etiologies have been proposed including amyloidosis, scleroderma, fibrosis, rheumatic fever, viral myocarditis, and coronary atherosclerosis,[51] most patients with the syndrome have no clearly identified etiology.

In a 7-year follow-up of 56 patients with sick sinus syndrome, Rubenstein et al[86] noted pacing was utilized in less than half of the patients for symptomatic bradycardia. In the absence of symptoms no pacing was required. Six deaths occurred over the 7-year follow-up period. Only one could be related to arrhythmia. This and other follow-up studies demonstrate the generally benign course of sinus node disease because cardiac sudden death is uncommon. Pacing is effective to alleviate symptoms but does not prevent mortality that occurs from other causes.[10] The most dangerous complication is cerebral embolism, which is not prevented by pacing.[28]

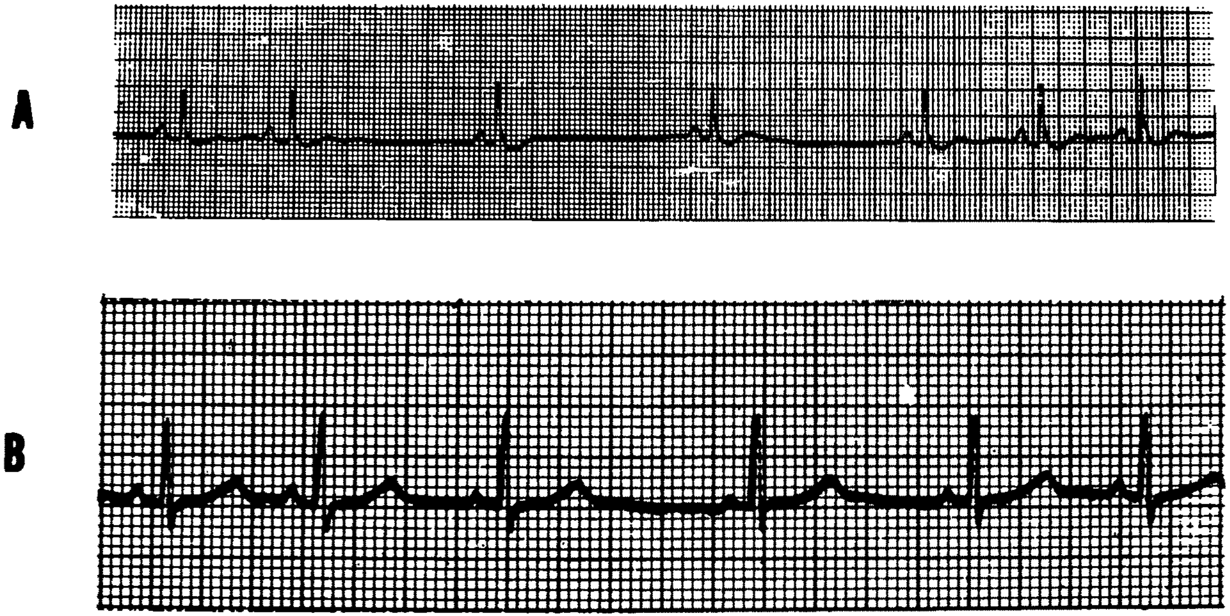

Figure 1. Sinus Rhythms. At first glance, the rhythm strips appear quite similar. Inspection of the P-to-P intervals reveals important differences. Tracing A shows sinoatrial exit block. Measurement of the P-to-P interval between the second, third, fourth, and fifth beats reveals that it is twice the length of P-to-P interval between the first and second beats. Sinus node depolarization (not visible on the ECG) is presumed regular, but the impulse is not conducted to the atrium between beats 2, 3, 4, and 5. Sinoatrial exit block may be seen in sick sinus syndrome and in normal persons. Tracing B shows a lengthening and shortening of the sinus cycle that is typical of respiratory influence on sinus rate. This is sinus arrhythmia.

The mechanism of the sinus bradycardia may be related to abnormal impulse formation or delayed conduction of the impulse out of the sinus node to the atrium.[45] Patients develop symptoms of syncope because a lower escape pacemaker fails to establish an adequate heart rate during periods of excessive bradycardia. Thus, sick sinus syndrome is a disease of the entire conduction system of the heart, rather than simply the sinus node. Often, other forms of conduction disturbance (AV block or bundle branch block) coexist.[68]

Ideally, the diagnosis of sick sinus syndrome can be made when symptoms (syncope or lightheadedness) correlate with episodes of bradycardia documented by ambulatory electrocardiography (Holter monitor). An inappropriate increase in heart rate to exercise, isoproterenol, or atropine[82] (heart rate less than 90 per minute after 1 mg intravenous atropine) suggests sick sinus syndrome. The presence of a slow atrial rhythm (nonsinus as evidenced by abnormal P waves in ECG leads II, III, aVF) may also suggest sinus node dysfunction.[30] Electrophysiologic studies can be helpful to evaluate sinus node function.[51] Reversible causes of bradycardia such as drug effects or hypothyroidism should be considered. Many antihypertensive agents (sympatholytic drugs),[88] beta blockers, calcium antagonists, antiarrhythmic agents, and antidepressants have been reported to worsen sinus node dysfunction. Pacemaker therapy is indicated for recurrent symptoms (for example, syncope) documented to be due to irreversible bradyarrhythmias.

Sinus bradycardia attributed to sick sinus syndrome in association with anesthesia has been reported in two cases (one spinal anesthesia,[100] one general anesthesia[14]). The diagnosis of sick sinus syndrome was made postoperatively when the patients experienced transient episodes of asystole. However, it is not clear that sick sinus syndrome was present. In the case of spinal anesthesia, the patient had preoperative syncopal symptoms related to vomiting. This suggests a vagal etiology of the postoperative arrhythmia. The case of general anesthesia had been complicated by intraoperative cardiac arrest first noted by the cessation of respiration. Because no ECG monitor was in place, it is possible that the arrest was due to ventricular fibrillation rather than asystole. The postoperative arrhythmia may have been related to the cardiac arrest.

Considering the prevalence of the disease, it is probable that patients with undiagnosed sick sinus syndrome have received general and regional anesthesia successfully. Preoperative evaluation of patients with known sick sinus syndrome should assess the patient's ability to physiologically increase heart rate because circumstances of hypotension and hypovolemia may be encountered during anesthesia and surgery. Patients can be divided into two groups depending on the etiology of the bradycardia.[46] In the first group of patients, the bradycardia is due to autonomic depression of automaticity or conduction (sinoatrial). These patients may respond to drug therapy such as hydralazine,[27, 105] prazosin, and aminophylline, which shift the autonomic tone toward sympathetic activation and parasympathetic withdrawal. Such patients can physiologically increase their sinus rate and can be identified by ambulatory Holter monitoring, exercise testing, or a challenge of intravenous atropine (1 to 2 mg).

The second group of patients has intrinsic disease[46] of the sinus node and will not increase their sinus rate even if autonomic tone is removed. Although their sinus rhythm may not respond to reflex activity, chronotropic agents such as isoproterenol may still speed up a subsidiary pacemaker (for example, junctional) and provide hemodynamic stability in urgent circumstances. These patients may need temporary pacing if a reliable response to isoproterenol is not obtained.

ATRIOVENTRICULAR BLOCK AND HIS BUNDLE ELECTROGRAM

AV block is described by the relationship of the P wave to the QRS complex on the surface ECG. First-degree AV block is characterized by a delay in one-to-one AV conduction, second-degree AV block by intermittent conduction, and third-degree AV block by absence of conduction of atrial impulses to the ventricle. Second-degree AV block is further subdivided into type I and type II depending on the nature of the intermittent conduction.

The His bundle electrogram[18, 19, 39, 81] has greatly facilitated the understanding of atrioventricular block by subdividing the PR interval into three subintervals (Fig. 2). The His bundle electrogram first records the atrial depolarization (A potential) at the end of intra-atrial conduction. The time between the start of the P wave on the surface ECG and the A potential is the PA interval and represents intra-atrial conduction time. The next impulse is the depolarization of the His bundle (H potential). This occurs after the AV node, so that the AH interval approximates conduction time through the node. The third interval HV is measured from the His potential to the beginning of ventricular depolarization on the standard ECG. The HV interval represents conduction time through the His Purkinje (bundle branch) system.

His bundle electrograms can be used to explain AV conduction[39, 81] delays (Table 1). First-degree AV block is typically due to a fixed, prolonged AH interval. Second-degree type I block is typically due to a progressive lengthening of the AH interval until an A potential is not followed by an H potential. Second-degree type II block typically shows constant AH intervals but intermittent block of conduction between the H and the V potentials. Third-degree AV block may occur either proximal or distal to the His bundle. In the first instance the QRS is preceded by an H deflection; in the second it is not.

In general, block in the higher regions of the conduction system is benign. No treatment is needed because lower subsidiary pacemakers can take over pacing function. Examples of benign conditions include block in the AV node (first-degree block, second-degree block

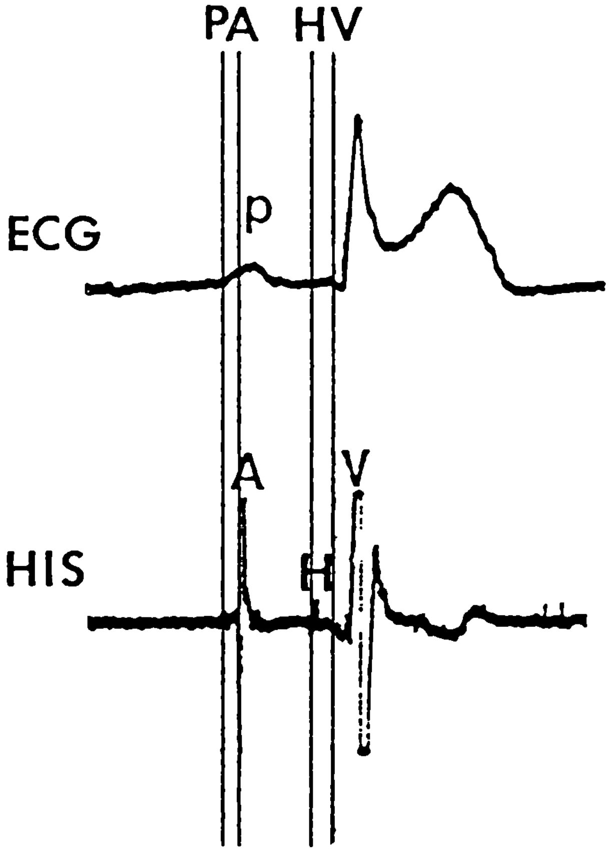

Figure 2. Electrophysiological intervals. The upper tracing is a standard surface electrocardiogram and the lower tracing is a simultaneous His bundle electrogram (His). The intra-atrial conduction time (PA interval) is measured from the onset of atrial depolarization on the surface ECG to the first rapid deflection on the His bundle electrogram. The AV node conduction time (AH interval) is measured from arrival of atrial depolarization (A) to the onset of the His potential (H). The conduction time through the His Purkinje system (including bundle branches) to the ventricles is measured from the His potential (H) to the onset of ventricular depolarization. This is the HV interval. Normal values are PA, 25 to 30 msec; AH, 60 to 140 msec; and HV 35 to 55 msec.

type I) and third-degree block proximal to His bundle. These conditions all have a normal QRS complex (see Table 1). In contrast, block in the lower regions of the conduction system (second-degree type II, and third-degree block distal to the His bundle) is potentially life-threatening since a subsidiary pacemaker may not arise or be stable. These conditions have an abnormal QRS complex.

FIRST-DEGREE ATRIOVENTRICULAR BLOCK

First-degree heart block is defined as a prolongation of the PR interval on the ECG. The PR interval begins at the start of atrial de-

Table 1. *Characteristics of Typical Atrioventricular Blocks*

ECG DEGREE OF BLOCK	QRS CONFIGURATION	HIS BUNDLE INTERVAL ABNORMALITY
First degree	Normal	AH: fixed, prolonged
Second degree type I	Normal	AH: progressive prolongation until block
Second degree type II	Abnormal	HV: intermittent block
Third degree	Normal	AH: complete block
Third degree	Abnormal	HV: complete block

polarization and ends at the beginning of ventricular depolarization. The PR interval describes conduction through the atrium, AV node, bundle of His, and the Purkinje fibers (bundle branches). The normally slow conduction velocity within the AV node accounts for a majority of the delay. This has been attributed to the AV node cells in the N region[64, 110] (densely packed central area). Characteristics of these cells include the slow upstroke of the action potential (dependent on the calcium current), high-resistance coupling between cells, and small cell diameter. The utility of the normal delay is to allow time for the atrium to empty into the ventricle and to protect the ventricle from rapid atrial rhythms.[62, 63] The normal adult value is up to 0.20 seconds but is less in children.[60] These normal values only apply to sinus rhythm because atrial pacing (without sympathetic stimulation) will prolong the PR interval at faster rates.[56]

By definition, a prolonged PR interval can be due to conduction delay in the atrium, the AV node, or the His Purkinje system.[69] By far the most common cause is delay in the AV node.[76] This usually represents enhanced vagal tone[12] or disease in the AV node. A physiologically prolonged PR interval is characteristic of the athletic heart.[55] In a study comparing 24-hour ambulatory ECG recordings in long-distance runners to recordings in healthy but untrained students, first-degree AV block occurred in 45 per cent of runners but only 8 per cent of untrained students.[97] In a study of 16,375 healthy male Air Force pilots, 350 cases of first-degree block were noted.[44] Examination in 139 of these pilots revealed medical disease in only five persons.

Uncommonly, prolongation of the PR interval can represent abnormal intra-atrial[70] conduction that may be suggested by markedly decreased P wave amplitude on the ECG. Also uncommonly, PR interval prolongation may be due to abnormal His Purkinje conduction, which may be suggested by an abnormal QRS configuration.[34, 77] This case has been termed trifascicular block since two fascicles (for example, the right bundle and the anterior division of the left) are abnormal and the delay in the PR interval is attributed to HV prolongation in the remaining fascicle (delay in left posterior division). However, even when only one fascicle remains to carry the cardiac impulse to the ventricles (such as with right bundle branch and left anterior hemiblock), a prolonged PR interval usually indicates delay in the AV node rather than the fascicle.[76] Thus, most cases termed "trifascicular block" are not trifascicular at all, but instead are bifascicular block with AV nodal conduction delay.His bundle studies may be required to rule out fascicular disease in such patients with symptoms of syncope.

The preoperative assessment of the patient with first-degree AV block should focus on the underlying cardiac condition. The vast majority of first-degree block is due to autonomic AV node delay and is benign.[17, 38, 102] In such cases, the PR interval should shorten with standing, exercise, atropine, or isoproterenol.[56] His bundle electrogram studies have shown that atropine[2] and isoproterenol[22] shorten the AH interval (but not the HV interval), confirming that their effect is to speed conduction in the AV node. If first-degree block occurs with bifascicular block in symptomatic patients (syncope), cardiology consultation should be obtained.[34]

SECOND-DEGREE ATRIOVENTRICULAR BLOCK TYPE I

Type I second-degree AV block (Wenckebach or Mobitz I) is characterized by a progressive prolongation of the PR interval until a P wave is blocked and not followed by a QRS complex (Fig. 3). The cycle then repeats. The PR interval following the dropped beat is the shortest of the sequence. The next PR interval shows the largest increment in length. Subsequent PR intervals become longer but by lesser and lesser amounts. This causes the R-to-R intervals to become progressively shorter after a dropped beat. The conduction ratio is described as the number of P waves to the number of QRS complexes per cycle (3:2, 4:3, and so forth). Longer cycles may not show a classic Wenckebach pattern,[21] but the PR interval following the blocked beat is always at least 20 msec shorter than the PR interval before the blocked P wave (Fig. 4). Knowledge of these details may help distinguish the benign Wenckebach block from the pathologic Mobitz II block.

Wenckebach AV block is not rare in persons with athletic training.[65] It is considered a benign arrhythmia when seen on the athlete's ECG.[55] In a 24-hour ECG study of 20 male long-distance runners, eight (40 per cent) were found to have episodes of Wenckebach block, most frequently during sleep.[97] In a control group of 50 healthy but untrained medical and dental students, only three demonstrated Wenckebach block during the 24-hour recordings. In a 6-year follow-up of three athletes with Wenckebach block, no heart disease or decreased athletic performance was found.[65] The etiology of the block in these cases is increased vagal tone that accompanies endurance training.

Wenckebach block has been associated with inferior wall myocardial infarction[42, 59] and may be due to parasympathetic activation by receptors in the ventricular wall (first hours of the infarction) or ischemia of the AV node[93, 96] (first days). The Wenckebach block is temporary and less likely to progress to complete heart block than is

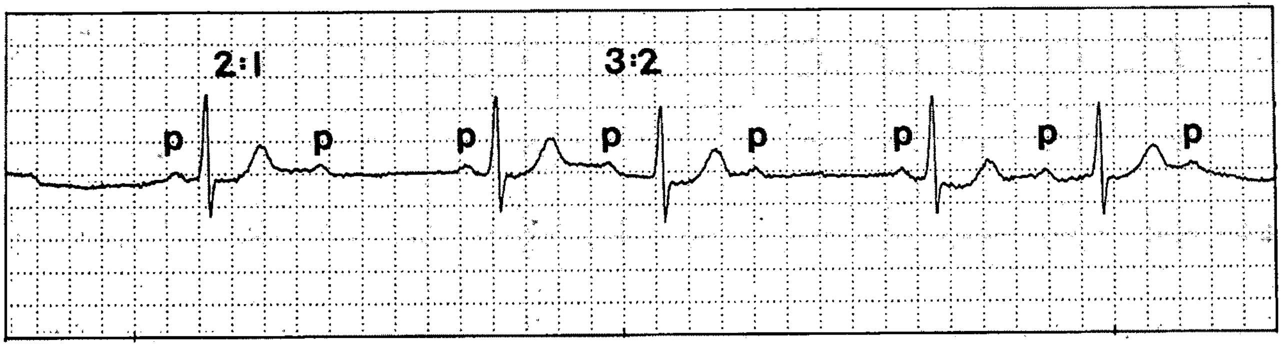

Figure 3. Second-degree AV block, Wenckebach type. Note the lengthening of the PR interval from the second QRS complex to the third QRS complex. The following P wave is not conducted to the ventricle. The cycle resumes with the next P wave. There are three P waves for two QRS complexes, so this is a 3:2 Wenckebach cycle. Note that the PR interval before the blocked P wave is greater than 20 msec longer than the PR interval after the blocked P wave. This differs from Mobitz II block where the PR interval is constant. Note also that the beginning of the tracing shows a period of 2:1 block. Without the subsequent changes in the PR interval, it would be impossible to define 2:1 block as Wenckebach or Mobitz II type.

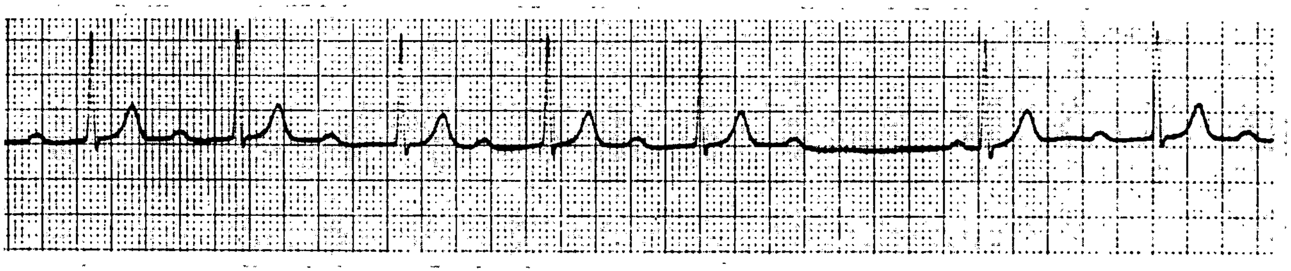

Figure 4. Nonclassic Wenckebach. During longer Wenckebach cycles, it is often difficult to see classic, progressive lengthening of the PR interval. However, examination of the PR interval after the blocked P wave demonstrates that it is the shortest of the cycle (always at least 20 msec shorter than the PR interval before the block).

Mobitz II second-degree AV block, which occurs with anterior myocardial infarction. If Wenckebach block in inferior myocardial infarction does progress to third-degree block, the site of the complete block is generally proximal to the His bundle[85] (the QRS is normal), leaving subsidiary pacemaker tissues intact.[71, 76, 82] Thus, Wenckebach block in myocardial infarction is not an indication for pacemaker placement in hemodynamically stable patients.

Wenckebach block occurring in children may progress to complete block.[108] A follow-up study of 16 children (aged 6 months to 17 years) with Wenckebach block demonstrated that seven developed complete heart block over several years of follow-up. However, each of these patients maintained a normal QRS complex and increased their heart rate with exercise, suggesting that the block was proximal to the His bundle. Only two patients had symptoms, and none died during the follow-up periods from 1 to 17 years after the onset of complete heart block.

His bundle electrogram analysis of typical Wenckebach block demonstrates a progressive lengthening of the AH interval, indicating conduction delay occurring in the AV node[18, 25, 39, 83] (Fig. 5). When block occurs, the A potential is not followed by an H potential. The electrical impulse did not reach the His bundle because it was blocked upstream in the AV node. Conduction is resumed in the next beat and its AH interval is the shortest of the cycle (analogous to the shortest PR interval on the ECG). The HV interval remains constant during conducted beats, indicating that conduction through the His Purkinje system is not the site of abnormality. The normal His Purkinje conduction delivers a synchronized impulse to the ventricles, resulting in a normal QRS complex.

Conduction through the AV node is markedly influenced by the autonomic nervous system. Carotid sinus massage, acetylcholine, and acetylcholinesterase inhibitors will worsen Wenckebach block.[57] Drugs that block the parasympathetic system (atropine) or mimic the sympathetic system (isoproterenol) will speed AV nodal conduction and abolish Wenckebach block due to AV nodal delay. Although the latter frequently occurs, occasionally there is such substantial sinus node acceleration that conduction block cannot normalize. In such cases, the site of block is not clear and His bundle recordings may be useful to determine the site of abnormality.[110]

In very unusual cases, a Wenckebach rhythm on the ECG has been attributed to an abnormality in the His Purkinje system.[76,110] A widened QRS on the ECG may be a clue to this situation. Since the His Purkinje system is not directly affected by atropine and isoproterenol, these agents will not improve this unusual etiology of Wenckebach block. In fact, atropine and isoproterenol may worsen block in the His Purkinje system due to their salutary effects on AV nodal conduction[57] (see section on Mobitz II block).

Second-degree AV block (type I or II) is rarely reported in studies of intraoperative arrhythmias. Vanik[101] reported only five episodes of second-degree block (four transient) in his study of 5013 patients

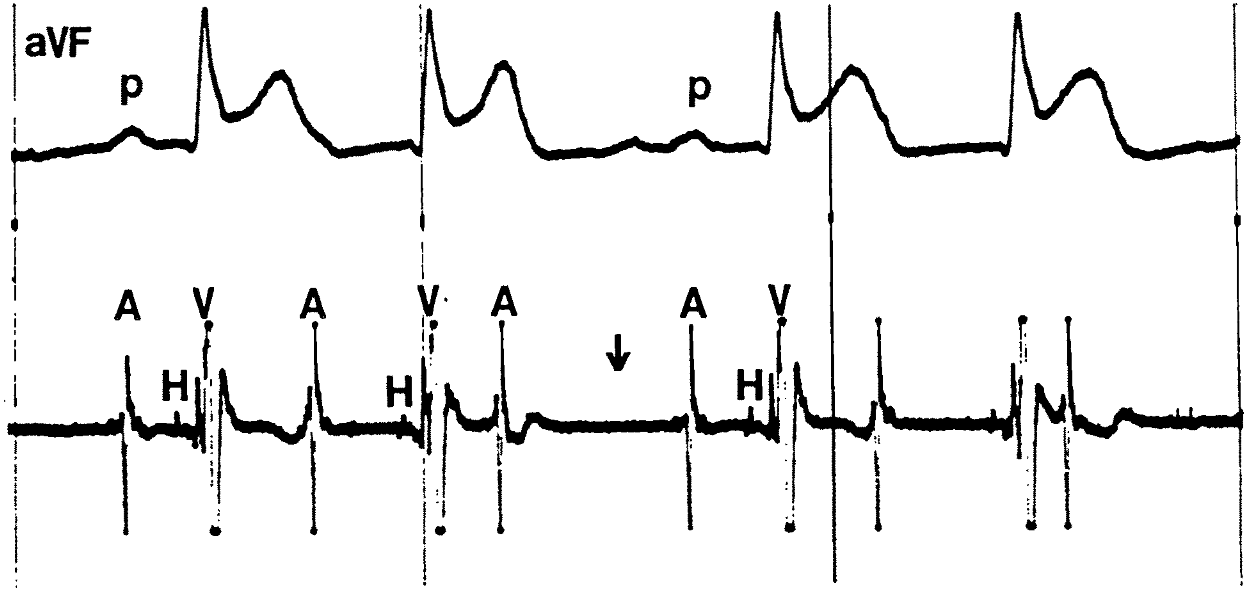

Figure 5. His bundle study of Wenckebach AV block. The upper tracing is standard ECG lead aVF and the lower trace a His bundle electrogram. The top trace clearly shows a P wave preceding the first QRS complex. This corresponds to the atrial depolarization (A) on the His bundle electrogram. The second and third P waves are obscured by T waves, but their location can be determined by the corresponding A potentials on the His bundle electrogram. Between the atrial depolarization (A) and ventricular depolarization (V), the His potential (H) can be seen. The distance between the A and H deflections represents conduction through the AV node. Note that the second AH interval is prolonged, as compared with the first AH interval indicating slowed conduction through the AV node. Finally, the third atrial depolarization (A) is not followed by a His potential (*arrow*), indicating blocking of conduction in the region of AV node.

undergoing halothane anesthesia, despite the fact that 118 of these patients were receiving digitalis. Dodd[24] reported that AV block occurred so infrequently that it was not possible to access its significance in his study of 596 patients under general anesthesia. Two recent case reports of arrhythmias occurring during anesthesia in athletes did not report the occurrence of second-degree AV block.[1, 13]

The preoperative assessment of a patient with Wenckebach block must focus on the underlying cardiac condition.[94] The athletic patient without cardiac symptoms probably requires no special therapy. Episodes of block will likely disappear with administration of atropine.[2] In contrast, Wenckebach block in acute inferior myocardial infarction is the result of cardiac disease that may be exacerbated by intraoperative events such as anemia, or pharmacologic therapy such as isoproterenol. It is not unreasonable to consider temporary pacing in such a patient scheduled for emergency surgery.[109]

SECOND-DEGREE ATRIOVENTRICULAR BLOCK TYPE II

In type II second-degree AV block (Mobitz II block), intermittent conduction of P waves to the ventricles occurs without changes in the PR interval (Fig. 6). There is no shortening of the PR interval after the dropped QRS, and the PR intervals remain constant during conducted, but abnormally widened, QRS complexes. A knowledge of these characteristics is useful to distinguish benign arrhythmias from Mobitz II block (Fig. 7).

Mobitz II block may occur after the progression of chronic underlying cardiac disease such as atherosclerosis, degenerative fibrosis of the conduction system (Lenegre's[53] disease and Lev's[54] disease), or cardiomyopathy. It can also acutely occur in anterior myocardial infarction.[93] Mobitz II block represents disease in the His Purkinje (bundle branch) system. Whether acute or chronic, this arrhythmia has a bad prognosis, because it is without a reliable subsidiary pacemaker in the ventricle. It may abruptly progress to complete heart block. Mobitz II block is an indication for pacemaker therapy even in asymptomatic patients.[66] Unlike Wenckebach block, no cases of Mobitz II block were found in 67,375 apparently healthy air force pilots[44] nor in a group of 20 male long-distance runners. Mobitz II block is not a characteristic of the athletic heart.[55]

The site of abnormality is almost always below the AV node in the His Purkinje system.[18, 25, 39, 81] His bundle studies demonstrate that the His potential follows the A potential correctly but that the His potential is not followed by the V potential at times of dropped beats (Fig. 8). When conduction to the ventricle is successful, the HV interval often is abnormally long in patients with Mobitz II block. Due to abnormal His Purkinje conduction, the QRS complex is often widened during conducted beats.

The response of Mobitz II block to drugs differs from Wenckebach block.[57] The His Purkinje system is not affected by atropine and iso-

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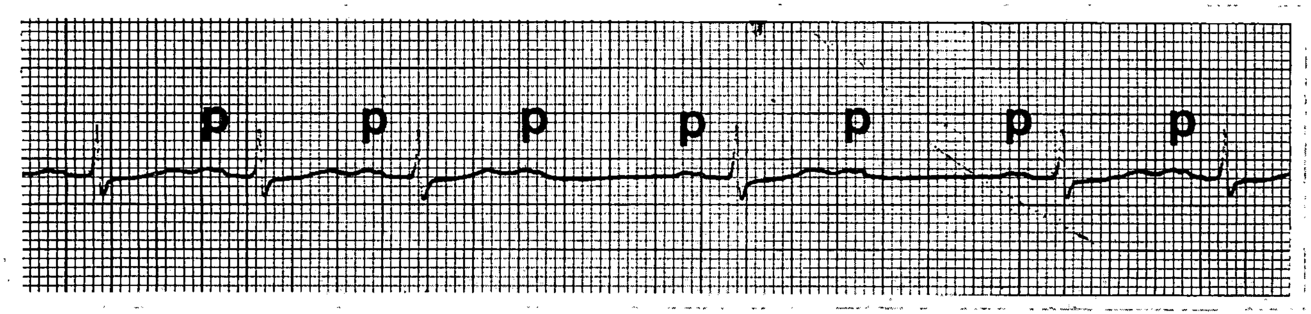

Figure 6. Second-degree AV block, Mobitz II type. Careful observation reveals a P wave after the T wave in beats 3 and 4. These P waves are not followed by a QRS complex. There is no lengthening of the PR interval prior to the blocked beats, and there is no shortening of the PR interval after the blocked P wave. This arrhythmia is Mobitz II block and suggests pathologic changes in conduction. It may be the harbinger of more severe heart block. Note the abnormal QRS associated with this rhythm. This tracing was from a Holter monitor of a patient who had syncopal episodes.

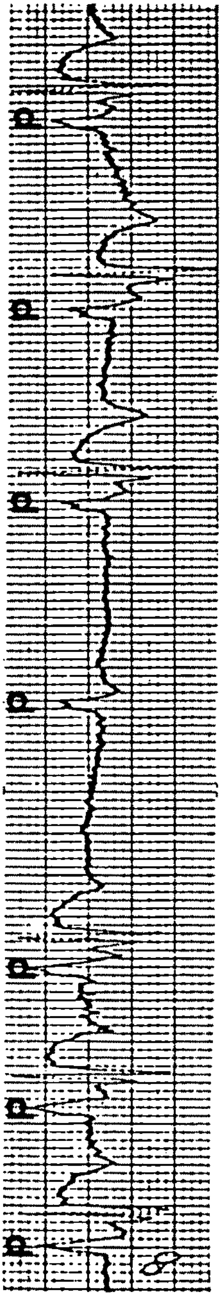

Figure 7. Vagal arrhythmia, not Mobitz II. At first glance, this rhythm strip appears to be Mobitz II block because it shows a blocked P wave without changes in the PR interval. Closer examination shows that the P-to-P interval changes, which is unusual for Mobitz II or for Wenckebach block. This rhythm is due to a burst of vagal tone that slowed the sinus rate (P-toP interval) and blocked conduction through the AV node.

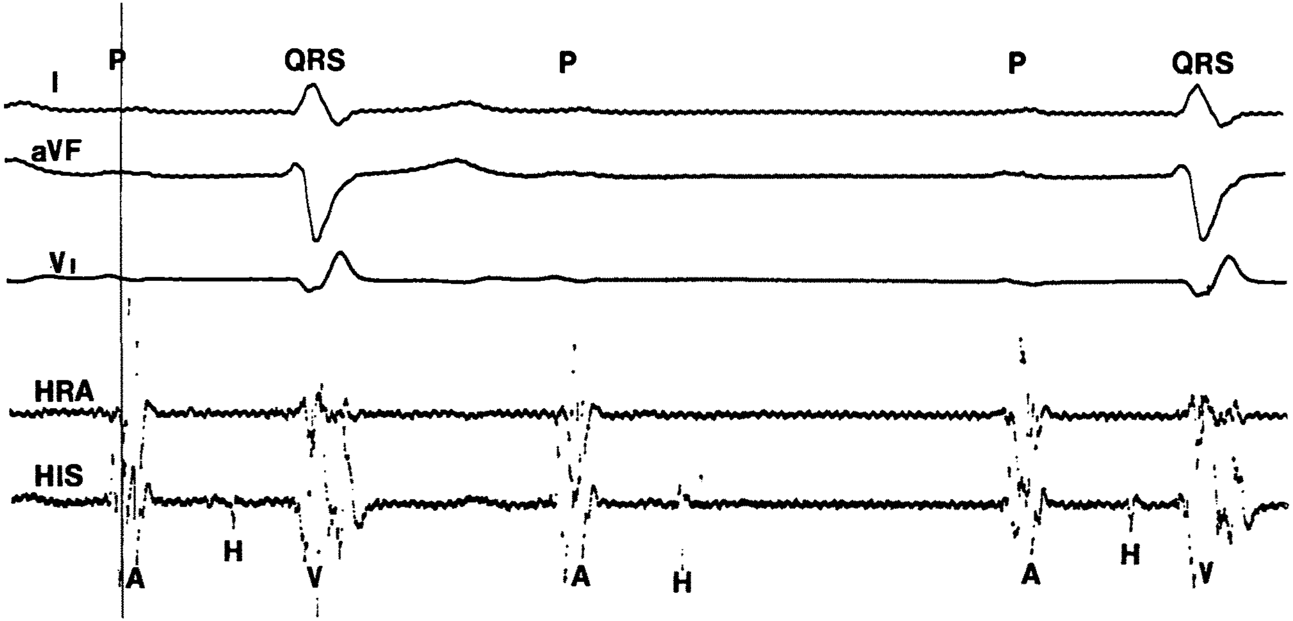

Figure 8. His bundle study of Mobitz II AV block. The upper tracings are standard ECG leads. The two lower tracings are taken from intracardiac electrodes in the high right atrium (HRA) and in the region of the His bundle (HIS) in a patient with Mobitz II AV block. The paper speed is four times the normal ECG speed. Atrial depolarization (A) is followed by a His potential (H) in each case, indicating that conduction through the AV node is satisfactory. However, after the second atrial and His bundle depolarization, there is no QRS (V potential). The block occurs after the His potential, indicating disease of the bundle branch system.

proterenol as is the AV node. In fact, atropine and isoproterenol may worsen Mobitz II block by increasing atrial rate and improving conduction through the AV node, which allows more frequent impulses to reach the abnormal His Purkinje system. These more frequent impulses will encounter the abnormal His Purkinje system and be blocked. In contrast, carotid sinus massage will slow conduction through the AV node, allow the His Purkinje system time to recover, and the conduction block may lessen. This behavior of type II block is opposite to that of type I and has been utilized to distinguish the site of block[57] when ECG diagnosis was not possible (such as 2:1 block).

As mentioned previously, second-degree AV block (type I or II) has been rarely reported in association with anesthesia.[24, 101] The occurrence of type II second-degree block in a preoperative patient is an indication for cardiology consultation and pacemaker placement. Pharmacologic therapy should not be relied on to improve hemodynamics, although it may be temporarily effective. Unless the surgery is urgent, thorough evaluation of the patient's cardiac status is indicated prior to operation.

THIRD-DEGREE ATRIOVENTRICULAR BLOCK

In complete AV block, none of the atrial depolarizations are conducted to the ventricles.[83] The P waves and QRS complexes are dissociated and the atrium and the ventricle beat at different rates according to their respective pacemaker tissues. High-grade AV block refers to blocked conduction of most but not all P waves. Conduction of an atrial beat to the ventricle interrupts the otherwise regular ventricular rate (Fig. 9). Block is considered complete when no conduction occurs despite every opportunity (every possible PR interval). Complete AV block may also be suspected when the ventricular rate is slow and regular during atrial fibrillation. This suggests that a subsidiary pacemaker is driving the ventricles rather than the irregular atrial impulses conducted through the AV node. This may be seen in digitalis toxicity.

Congenital chronic heart block may be due to the developmental failure of the AV node to connect to the atrium or the His Purkinje system.[3] Congenital chronic third-degree heart block can be divided into two groups depending on the site of conduction block.[84] A block below the bundle of His shows a widened QRS and is characterized by a slow pacemaker that does not respond to exercise or autonomic drugs.[76] Such patients are likely to experience syncopal symptoms, exercise intolerance, and congestive heart failure.[67] Pacemaker therapy is helpful to relieve symptoms.[99]

In contrast, block above the bundle of His is characterized by a narrow QRS and a faster pacemaker that does respond to exercise and autonomic drugs.[49] These patients often have good exercise tolerance, no symptoms of syncope or failure, and do not require pacemaker

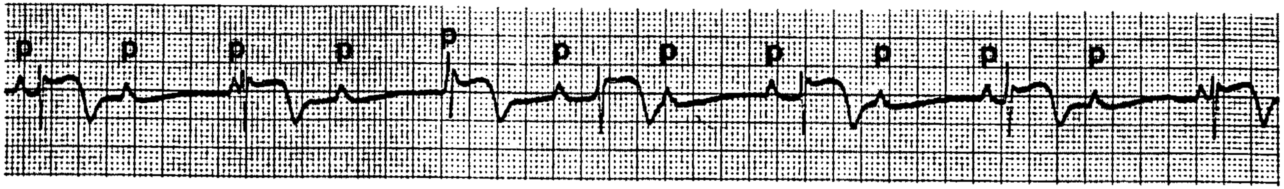

Figure 9. High-grade AV block in acute myocardial infarction. This tracing shows P waves occurring regularly but not related to the QRS complexes. The ventricular depolarization occurs because a lower, subsidiary pacemaker tissue has taken over the pacing function. The narrow QRS suggests that this pacemaker is above the ventricles such as the AV node. Note that the fourth QRS comes earlier than expected. This indicates that the preceding P wave was conducted to the ventricles. True third-degree AV block should have no such episodes of conduction; hence this tracing is termed high-grade AV block.

placement. An electrophysiologic study in children with third-degree heart block showed that if block was in the AV node, the average resting ventricular rate was 60. If the site of block was below the His bundle, the average ventricular rate was 44.[75]

There are several reports of anesthesia for children with congenital complete heart block.[23, 26, 73] In each of these cases, the patients lacked episodes of syncope, had good preoperative exercise tolerance, had normal QRS duration, and increased their ventricular heart rate with atropine. All of these patients tolerated general anesthesia well without the need of cardiac pacing. Some authors utilized drugs known to cause tachycardia (ketamine, gallamine), whereas others successfully used thiopental, succinylcholine, fentanyl, and halothane. These cases illustrate complete heart block with a subsidiary pacemaker high in the conduction system.

Acquired complete heart block may result from myocardial infarction, drug toxicity, electrolyte imbalance (hyperkalemia, hypermagnesemia), cardiac surgery,[111] systemic diseases (amyloidosis, sarcoidosis, scleroderma, polymyositis), and fibrosis of the conduction system. As with congenital heart block, the site of the block can be proximal or distal to the His bundle.

Patients with block proximal to the bundle of His (inferior myocardial infarction[76, 85]) demonstrate a narrow QRS complex, adequate heart rates, lack of symptoms, and respond to atropine with an increase in heart rate. These patients have a reliable subsidiary pacemaker high in the conduction system. In contrast, most cases of acquired third-degree heart block are due to a block distal to the His bundle (anterior myocardial infarction,[76, 85] bilateral bundle branch disease, post congenital cardiac surgery).[84] These patients demonstrate an escape rhythm with a widened QRS complex, slow heart rates, symptoms of poor perfusion (syncope and fatigue), and little response to atropine. These patients have an inadequate subsidiary pacemaker. Their cardiac output is low at rest and fails to rise with exercise[90] as evidenced by a widened AV oxygen extraction. Since heart rate is fixed, maintenance of cardiac output depends on high filling pressures to maximize stroke volume by the Starling mechanism.

The preoperative assessment of the patient with complete heart block should determine the site of the block in the conduction system. Asymptomatic patients who have good exercise tolerance, narrow QRS complex, and normal resting heart rates (60 per minute) probably have the site of block above the His bundle. These patients have a reliable subsidiary pacemaker that should respond to autonomic drugs.[49, 76] These patients should tolerate anesthesia well.

In contrast, the patient with symptoms of syncope or fatigue, widened QRS complex, and slow heart rate (40 per minute) that fails to increase with autonomic drugs probably has the site of block below the His bundle.[49, 76] Pacemaker placement should be considered in these patients because their escape pacemaker may be unreliable. Such patients with a fixed, low cardiac output will respond poorly to hypovolemia, anemia, or reduction in arterial oxygenation. Drug elimination may be reduced owing to decreased renal[20, 41] and hepatic[90] blood flow. Although electrical pacing will improve the heart rate, additional cardiac output may be obtained with inotropic agents.

One important caveat must be made in regard to the diagnosis of third-degree heart block.[60] Junctional tachycardia must be distinguished from third-degree block. In complete heart block, atrial rates range from 80 to 120 per minute and ventricular rates are 70 per minute or lower. Whenever the ventricular rate exceeds 70 per minute from a junctional pacemaker, retrograde conduction to the AV node (concealed conduction) may be the cause of the AV conduction impairment. Cardiology consultation should be obtained to confirm this possibility because no abnormality of AV conduction may be present in junctional tachycardia.

EFFECTS OF ANESTHESIA AND SURGERY

Anesthetic agents and surgery can affect the autonomic nervous system and thereby affect cardiac rate and conduction. The sympathetic system can be stimulated by pain, hypovolemia, anemia, or mimicked by drugs such as ephedrine. The sympathetic system can be blocked centrally by general anesthesia or regionally by local anesthetics (spinal). The parasympathetic system can be stimulated by fear, surgical traction (for example, ocular muscles), laryngoscopy, or mimicked by drugs such as anticholinesterase inhibitors. Fentanyl bradycardia has been attributed to a central vagal stimulation since vagotomy prevented the bradycardic effect in a dog model.[79] The parasympathetic system may be blocked by anticholinergic agents used for their sedative or antisialogue effects. Pancuronium has been shown to have a vagolytic effect to facilitate conduction through the AV node.[11, 32] Since cardiac rate and conduction are influenced by the autonomic nervous system, intraoperative changes can be anticipated.

The possibility that anesthetic agents directly affect cardiac rate has been investigated. There is evidence of direct effects of inhalation anesthetics on heart rate. In isolated guinea pig preparations, Bosnjak[9] has shown that halothane, enflurane, and isoflurane slowed the rate of sinus node discharge due to a reduction in the slope of phase 4 depolarization. However, in normal human volunteers, enflurane[15] and isoflurane[95] have been shown to cause tachycardia, and halothane[92] to cause little change in heart rate. This probably represents the overriding influence of the autonomic nervous system. The findings of Bosnjak may explain the appearance of junctional rhythms during anesthesia and may be important for those patients with sick sinus syndrome who have impaired ability to activate subsidiary pacemakers.

Succinylcholine has also been associated with slowing of sinus rhythm.[61, 106] The bradycardic effect of succinylcholine, particularly with multiple doses, has been reported. The effect on sinus node appears due to the metabolite, since succinylcholine and its metabolite succinylmonocholine caused a tachycardia and bradycardia, respectively, when infused to the isolated sinus nodal artery in a guinea pig preparation.[107]

The possibility of direct effects of inhalation agents on cardiac conduction has also been investigated. In dogs, Atlee et al[4, 5] have shown that halothane, enflurane, and isoflurane prolonged AV nodal conduction time and to a lesser extent, His Purkinje conduction time. However, after autonomic blockade with atropine and propranolol, there was no significant effect of anesthetic. The authors concluded *that* the changes in conduction were due to indirect autonomic effects rather than direct effects of the anesthetics.[6] These conclusions are supported by Santini et al,[87] who studied the effects of anesthesia on 20 patients with various conduction defects (right bundle branch block, left bundle branch block, bifascicular block, and so forth). Nineteen of these patients had symptoms of dizziness or syncope. His bundle electrograms were recorded prior to anesthesia and then following (1) atropine, (2) thiopental, (3) succinylcholine, (4) halothane in nitrous oxide and oxygen, and (5) enflurane. In the majority of the patients, there were no significant changes in the conduction intervals. Three cases of temporary second-degree AV block occurred several minutes after succinylcholine. The authors concluded that general anesthesia does not significantly affect cardiac impulse conduction in the majority of symptomatic patients with known conduction defects. The authors advised caution in the use of succinylcholine in symptomatic patients with syncopal episodes.

Further evidence of the safety of anesthesia in patients with bundle branch block is provided by three studies: Berg and Kotler[7] studied 20 patients with bilateral bundle branch block; Rooney[80] studied 27 patients with right bundle branch block and left axis; and Pastore et al[74] studied 44 patients with right bundle branch block and left axis. Only one episode of documented complete heart block occurred when general, spinal, or regional anesthesia was performed. Pastore reported that this single episode appeared at the time of intubation and responded to temporary pacing. All of these authors concluded that temporary pacing is rarely required in preoperative patients with bundle branch block.

Thus, although there are some potential direct effects of anesthetic agents on cardiac rate and conduction, the predominant influence appears to be indirect from changes in the autonomic nervous system.

INTRAOPERATIVE MANAGEMENT

The anesthesiologist can prepare for intraoperative problems by knowledge of the arrhythmia, its subsidiary pacemaker and its expected response to drugs. Intraoperative monitoring is critical to apply that knowledge quickly and appropriately. The electrocardiogram is the standard monitor for diagnosis of rhythm changes. Occasionally, other monitors are also helpful. The sudden appearance of cannon A waves in a central venous pressure tracing is often the clearest indication of the onset of a junctional rhythm[35, 52] (Fig. 10). Sometimes the electrocardiogram does not clearly show P waves to allow the diagnosis. In these circumstances, electrical activity directly from the

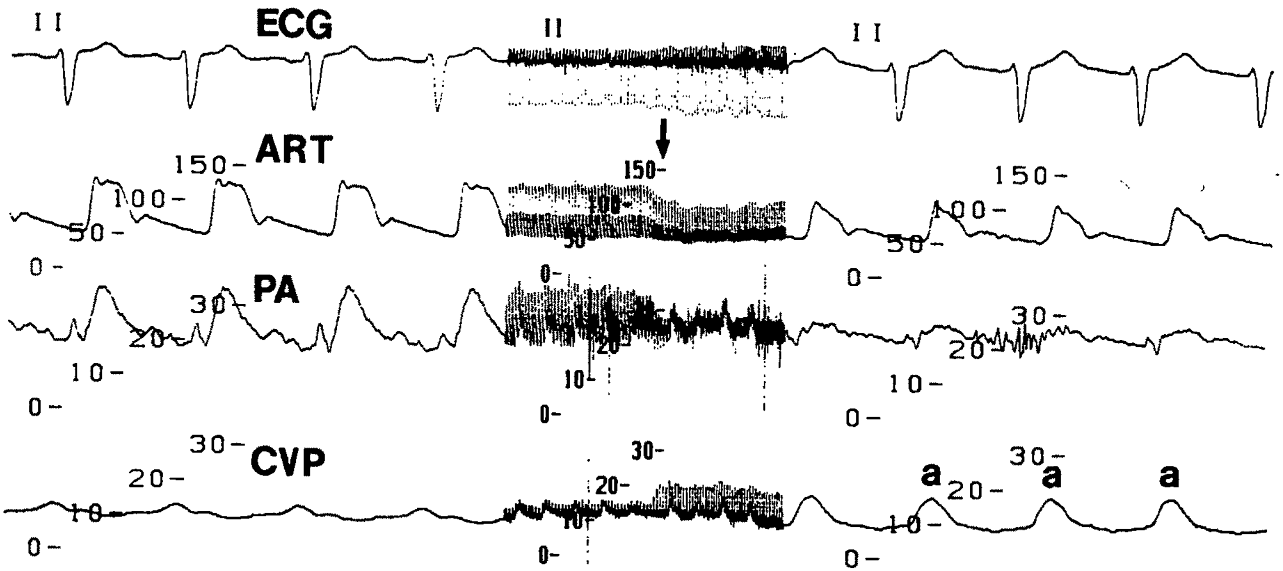

Figure 10. Cannon A waves. The tracings represent (top to bottom) ECG, arterial blood pressure (ART), pulmonary artery pressure (PA), and central venous pressure (CVP). At the arrow, an abrupt drop in blood pressure occurs. The rhythm has changed from sinus to junctional with a loss of atrial contribution to ventricular filling. The clearest signal of the junctional rhythm is the appearance of the cannon A waves in the CVP, coincident with the blood pressure drop. Note that the ECG alone is not helpful because the P waves are poorly described.

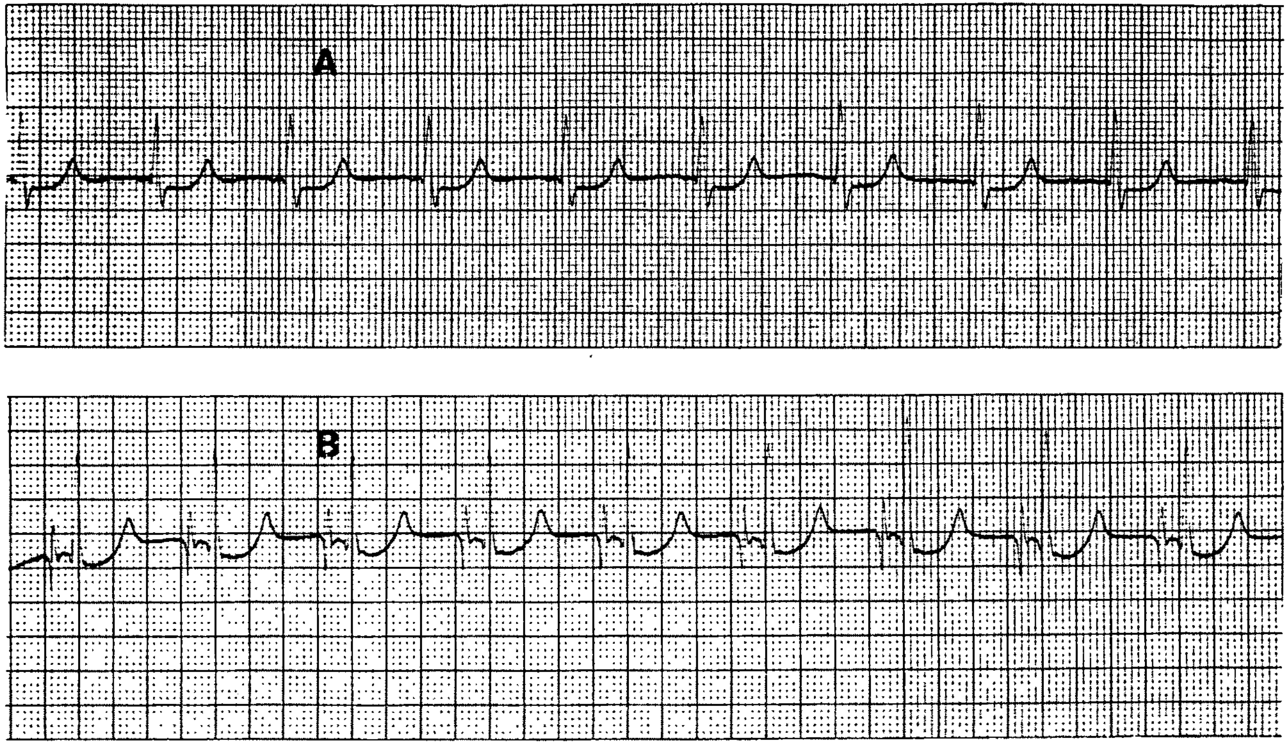

Figure 11. The atrial electrogram. These tracings (both lead II) were taken from a patient after arrival in the intensive care unit following cardiac surgery. Tracing A appeared to show a junctional rhythm. By connecting one of the temporary epicardial atrial pacing wires to the ECG (a unipolar recording), tracing B was generated. The augmented atrial tracing clearly makes the diagnosis of an atrial, not junctional, rhythm because each QRS is preceded by a biphasic P wave.

atrium (atrial electrogram) can be obtained by an esophageal electrode[36, 47] or the atrial pacing wires[103] in cardiac surgery patients (Fig. 11). Pulse oximetry is also an ideal monitor because it measures perfusion (as compared with the ECG, which measures only electrical events). Since the first priority for any intraoperative bradycardia is to rule out hypoxemia, the pulse oximeter should be utilized in any patient who is prone to bradycardia.

A second goal of monitoring is to assess the adequacy of cardiac output in patients who have a limited ability to increase their heart rate. Patients with third-degree heart block distal to the His bundle constitute such a group. Their cardiac output may be relatively fixed and unable to compensate for circumstances such as hypovolemia, anemia, or a decrease in arterial oxygenation. Monitors of body perfusion include examination of the extremities for color and temperature, urine output, and arterial blood gas analysis for the appearance of metabolic acidosis. Management for such patients will include a high inspired oxygen delivery and maintenance of hematocrit and filling pressures. Electrical pacing of the heart may significantly improve the cardiac output.[20, 41, 89] Additional measures to treat inadequate perfusion may include inotropic drugs to augment contractility.

SUMMARY

There are several concerns when a patient with bradycardia or conduction abnormalities must undergo anesthesia and surgery. First is the possibility that the arrhythmia will worsen intraoperatively. A second concern is whether pharmacologic interventions would be effective if hemodynamic instability occurs. A third concern is whether a pacemaker should be placed preoperatively or whether standby facilities[31, 72] (external pacing)[111] are sufficient. A knowledge of the site of the arrhythmia, its expected physiology and natural history can be of help to answer these concerns. Conduction disturbances high in the system (such as AV node) generally are benign since they do not progress to more severe conduction blockade, they respond to pharmacologic agents such as atropine and isoproterenol, and their escape pacemaker is fast enough to maintain hemodynamic stability. Disturbances lower in the system are rare, more pathologic, and frequently result in hemodynamic instability. The individual arrhythmias of sick sinus syndrome, first-degree, second-degree, and third-degree AV block have been discussed. It is hoped that this discussion will aid in the planning of a safe intraoperative course for patients with these disorders.

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Arrhythmias Common to Infants and Children

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Very little attention has been paid to arrhythmias in the pediatric population until recently. This is probably due to the fact that arrhythmias have been considered relatively rare outside the operating room in a population that is for the most part "healthy." However, anesthesiologists have been aware for many years of the propensity of the pediatric patient to develop arrhythmias during anesthesia. Anesthesiologists are caring for an increasing number of pediatric patients presenting for surgery with a diagnosis of one form of arrhythmia or another. Many factors account for this, including improved detection of fetal arrhythmias, increased survival rate of premature infants, and improved surgical techniques, and hence, survival of infants with congenital heart disease.

This article discusses a wide range of arrhythmias present in this pediatric population including arrhythmias diagnosed during the fetal period, inherited or acquired disorders, common intraoperative arrhythmias, and those arrhythmias commonly present following surgical correction of congenital heart defects.

DEVELOPMENT OF THE FETAL CONDUCTION SYSTEM

In any discussion of pediatric arrhythmias, including those diagnosed in the gestational period, a brief discussion of the growth and development of the fetal conduction system is necessary.

The human heart has attained most of its adult characteristics by the sixth to eighth week, and the conduction system seems to be functional by the 16 week. The sinus node is recognizable by the sixth gestational week and is formed in the primitive sinus venosus. This corresponds to the region of the ostia of the two vena cavae, the ostia

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of the coronary sinus and the sinus intercavarum. In the early stages of development the sinus node artery is present as a proximal branch of either the right (about 55 per cent) coronary artery or the left circumflex (45 per cent).[15]

The atrioventricular node (AV) node is nearly formed by the tenth gestational week. The AV node and His bundle originate in separate areas and are united at the eighth week.[31]

The human heart has three pathways with connections between the sinus node and the AV node: the anterior, middle, and posterior internodal pathways. There is one pathway that connects the sinus node to the left atrium. These pathways are composed of a mixture of Purkinje cells and cells that resemble normal myocardium. Conduction in these pathways is more rapid than in the adjacent myocardium but not as rapid as conduction via the His bundle.[15]

FETAL CARDIAC ARRHYTHMIAS

With the advent of electronic fetal monitoring, detection and the antepartum treatment of fetal cardiac arrhythmias is becoming more widespread.[31] The diagnosis of fetal arrhythmias with or without treatment may profoundly affect the anesthetic course of the neonate presenting for surgery. Also, the anesthesiologist dealing with obstetric patients should have an understanding of fetal arrhythmias, their causes, and the correlation with congenital heart disease and fetal morbidity. Cardiac arrhythmias in the gestational period are classified similar to those in the newborn or pediatric population: (1) disorders of the sinus node: sinus bradycardia or tachycardia, sinus arrhythmias, sinoatrial block, escape rhythms; (2) supraventricular arrhythmias: premature supraventricular beats, supraventricular tachycardia, atrial flutter and/or fibrillation; (3) AV block; and (4) ventricular arrhythmias: premature ventricular beats, ventricular tachycardia and/or fibrillation.

Disorders of the Sinus Node and Supraventricular Arrhythmias

Fetal sinus tachycardia is defined as a rate greater than 180 beats per minute. There is almost always a variability of 5 to 15 beats per minute as opposed to supraventricular tachycardia (SVT) where the RR interval is usually fixed. Causes of sinus tachycardia are multiple and include maternal anxiety or fever, amnionitis, cytomegalic inclusion diseases, administration of atropine, and early fetal hypoxia.[31]

Fetal sinus bradycardia is defined as a heart rate less than 100 beats per minute with P waves and normal AV conduction. Causes include fetal head or umbilical cord compression, maternal hypotension, maternal seizures, maternal voiding, paracervical block, and propranolol or reserpine administration.[31]

Sinus arrhythmia or variability is caused by the fetal autonomic nervous system modifying the heart rate and is usually a sign that the

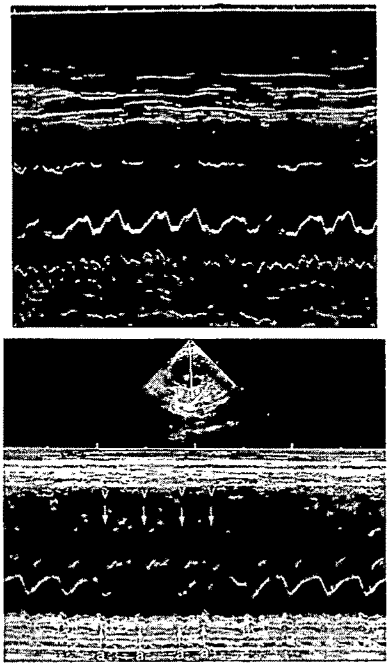

Figure 1. M-mode echocardiogram of fetus, in utero, showing atrial tachycardia with variable ventricular response and conversion to sinus rhythm after treatment of the mother with digoxin. (Tracings courtesy of Ed Colvin, MD, U.A.B. Department of Pediatric Cardiology.)

fetus is doing well. Drugs affecting variability include diazepam, meperidine, morphine, atropine, and scopolamine.[31]

Sinoatrial block occurs with strong parasympathetic input, as seen with severe umbilical cord or head compression. The heart rate may fall 60 or more beats per minute with decreased amplitude or disappearance of the P wave. Escape beats usually occur in the AV node but may occur anywhere in the atrial conduction system. The escape beats may be lifesaving if the sinus arrest is prolonged. There is controversy as to whether or not atropine should be administered in these situations.[31]

Premature atrial contractions occur in approximately 3 to 10 per cent of normal fetuses and are generally considered benign.[31]

Supraventricular tachycardia is a nonvariable tachycardia with a rate that usually exceeds 200 beats per minute (Fig. 1). Some degree of congestive heart failure (CHF) may be present in the fetus and if near term, labor may be induced or cesarean section performed to facilitate treatment. The newborn with persistent SVT is usually treated with electrical cardioversion, quinidine, or digitalis. The incidence of congenital heart disease is 5 to 10 per cent when persistent

SVT is present. Fetal SVT will be covered in more detail when SVT is specifically discussed later in the article.

Atrial flutter or fibrillation in the fetus is extremely rare but may be potentially serious if associated with congenital heart disease. In atrial flutter the atrial rate is usually 300 to 460 beats per minute with variable AV block and ventricular rates of 60 to 200 beats per minute. Atrial fibrillation shows the characteristic irregular atrial activity with variable ventricular response. Fetal CHF is rare with these arrhythmias in the absence of additional cardiac pathology. Digitalis and electrical cardioversion are the usual modes of treatment in the newborn and the prognosis is good if congenital heart disease is not present.

Ventricular Arrhythmias

Ventricular arrhythmias in the fetus are extremly rare and may or may not be associated with congenital heart disease. Antepartum treatment of PVCs or ventricular tachycardia is still a point for debate and fetal ventricular fibrillation has not been reported.

INHERITED OR ACQUIRED ARRHYTHMIAS

Although inherited or acquired arrhythmias are often diagnosed and treated in the preoperative period, their presence may profoundly affect intraoperative management. For this reason it is appropriate to discuss these disorders in some detail.

In dealing with the pediatric population one soon realizes that "normal" heart rates vary significantly with respect to age, generally decreasing with increasing age. Normal awake resting heart rate for the newborn and neonate may be as low as 100 or as high as 200, and 60 to 120 at about 10 years of age. Sleeping "normals" are 20 to 30 per cent lower and exercise "normals," 20 to 30 per cent higher.

Sinus Bradycardia

Congenital isolated sinus bradycardia in infants is very rare but it is well known that infants often respond in a "vagal fashion" to various stimuli. Systemic disorders such as hypoxia, acidosis, and increased intracranial pressure are particularly likely to cause bradycardia.[9] Bradycardia may be noted after operation for congenital cardiac defects secondary to injury to the sinus node and may occur immediately postoperatively or years later. Approximately 10 to 20 per cent of patients with sinus node damage will present to the operating room for pacemaker placement.[33]

Heart Block

Heart block may be defined as any slowing or cessation in the conduction of impulses from the sinus node to the AV node. Heart block is commonly divided into first degree, second degree (Mobitz I and II), and third degree, or complete heart block.

First-degree block, as in adults, is usually a benign entity and is manifested as a prolongation of the PR interval. It is seen in association with acute rheumatic fever, digitalis intoxication, viral myocarditis, Kawasaki's disease, Ebstein's anomaly, L-transposition of the great arteries, primum and secundum atrial septal defects, and after surgery for congenital heart defects.[33] Usually, the block is in the AV node but may be anywhere in the conduction system from atrial muscle to the bundle branch system.[3] If the block is not in the AV node it is usually associated with congenital heart disease or postoperative damage.[9, 33]

Second-degree heart block may be classified as either type I (Wenckebach) or type II. The most common form in children is Wenckebach AV block. The block is almost exclusively in the AV node and is generally considered benign but rarely may progress to complete heart block.

Type II AV block is generally considered more serious and usually denotes pathology in the conduction system distal to the His bundle. It is unusual to see type II AV block in pediatric patients but if present it may progress to complete heart block.[33]

Third-degree, or complete AV block, is the most common cause of persistent significant bradycardia in children. It may be either congenital or acquired, with the acquired group being divided into surgical or nonsurgical causes. Congenital complete heart block occurs in approximately one in 20,000 live births. It has been associated with cardiac tumors, myocarditis, endocardial fibroelastosis, L-transposition of the great arteries, asplenia-polysplenia syndrome, and connective tissue disease in the mother.[33] The patients at greatest risk for death in the first year of life are those with atrial rates above 140 beats per minute and ventricular rates less than 55 beats per minute.[9] Children who manifest CHF (usually with rates less than 50 beats per minute) require cardiac pacing. Several drugs may be of use in raising the heart rate until temporary pacing, either transvenous or transthoracic, can be instituted. Intramuscular or intravenous ephedrine (0.05 to 0.1 mg per kg) or epinephrine (0.1 to 1.0 μg per kg) are useful acutely, and for more continuous regulation, isoproterenol infusion titrated to effect (0.025 to 0.1) μg per kg per minute). Only a small percentage of patients with congenital complete heart block require permanent pacing.[33]

Complete heart block following surgery may occur immediately postoperatively or not until many years later (Fig. 2). It most commonly has followed correction of ventricular septal defect (VSD), tetralogy of Fallot, and AV canal. Postsurgical complete heart block is usually treated with a permanent pacemaker because of a significant incidence of sudden death.

Sick Sinus Syndrome

Sick sinus syndrome is a well-known entity characterized by paroxysms of both tachyarrhythmias and bradyarrhythmias, hence the common term "tachy-brady syndrome." Disorders of sinus node au-

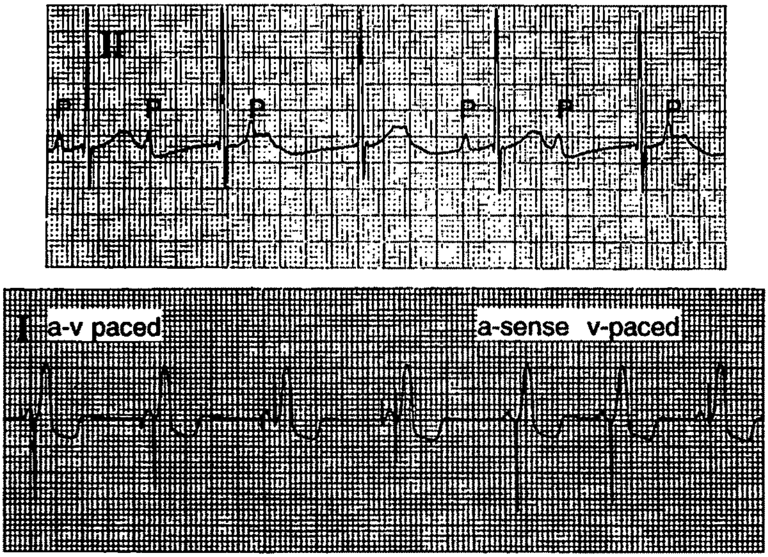

Figure 2. Complete heart block following surgical repair of complex VSD; treated with permanent epicardial AV pacer. (Tracings courtesy of Ed Colvin, MD, U.A.B. Department of Pediatric Cardiology.)

tomaticity, or conduction through atrial tissue, have both been implicated as possible causes. Sick sinus syndrome is not an uncommon sequela following surgery for congenital heart disease, especially transposition of the great vessels and sinus venosus ASD.[10, 25] There is also evidence to suggest that some families may exhibit an autosomal dominant inheritance pattern.[13]

Sick sinus syndrome is characterized by an abnormally functioning sinus node with bradycardia followed by escape tachyarrhythmias from either an atrial or AV nodal focus. The tachyarrhythmia further suppresses sinus impulses through overdrive suppression. Syncope or death may result when the tachyarrhythmia stops and there is a period with no pacemaker input from any source.[9, 10] Arrhythmias described with SSS include atrial fibrillation and flutter, with ectopic and junctional rhythms also being seen.[25]

The current treatment includes insertion of a permanent pacer in symptomatic children prior to initiating therapy for the tachyarrhythmias for fear of aggravating sinus node dysfunction or AV node conduction with drugs such as digoxin, quinidine, or procainamide.[9, 25] In fact, the incidence of tachyarrhythmias may be greatly reduced following pacemaker placement alone, removing the necessity for further pharmacologic treatment.[9]

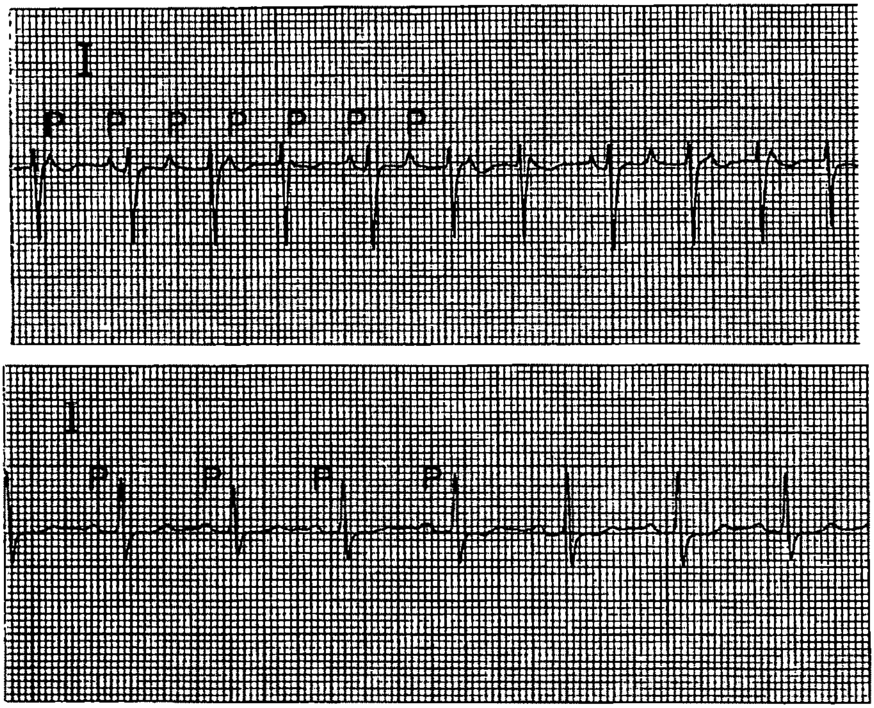

Figure 3. ECG tracing of 13-year-old male with a structurally normal heart demonstrating incessant atrial ectopic tachycardia (atrial rate 160, ventricular rate about 120 with Wenckebach). Unresponsive to digoxin but converted with flecainide. (Tracings courtesy of Ed Colvin, MD, U.A.B. Department of Pediatric Cardiology.)

Supraventricular Tachycardia

Supraventricular tachycardia is the most common arrhythmia noted in the pediatric age group[33] (Figs. 3 and 4). It has been estimated to occur in more than 1 in 25,000 children and is more common in males in the first few months of life.[25] It is known that there is significant postnatal molding in the region surrounding the AV node and His bundle with direct accessory pathways being normal in the newborn heart. This may in part account for the fact that re-entry seems to be responsible for most cases of SVT in children. Predisposing factors include infection, fever, drug exposure, Wolff-Parkinson-White syndrome, and congenital heart disease. Ventricular septal defect, Ebstein's anomaly, corrected transposition of the great arteries, and cardiomyopathy are the most common preoperative lesions with d-transposition of the great arteries, atrial septal defects, and AV canal defects being the most common postoperative lesions.[33]

Eight mechanisms of SVT have been described in children and include (in decreasing order of frequency) AV-node re-entry, atrial ectopic tachycardia, re-entry through a manifest bypass tract, SA-node

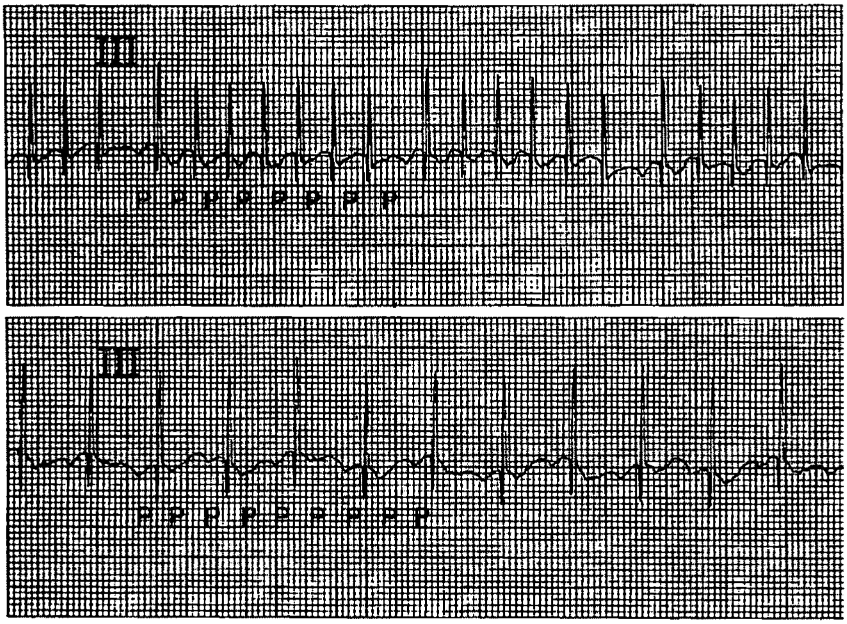

Figure 4. ECG tracing of 19-month-old male, 16 months postoperatively. Senning repair of transposition. Atrial tachycardia of a few days duration (atrial rate 260, ventricular rate about 250). Note that this pediatric atrial tachycardia does not break following the nonconducted P wave. Digoxin therapy resulted in 2:1 block with rate control (approximately 125 per minute). (Tracings courtesy of Ed Colvin, MD, U.A.B. Department of Pediatric Cardiology.)

re-entry, re-entry through a concealed bypass tract, re-entry through AV nodal bypass tracts, and junctional ectopic tachycardia.[33]

As mentioned previously, SVT may be detected in utero and does predispose to CHF. Also, there is a greater incidence of cardiac decompensation after delivery.[2] Several drugs that cross the placenta have been given to the mother during the gestational period in an attempt to convert the fetal heart to a normal sinus rhythm. Digitalis, calcium antagonists, and beta blockers have been tried with mixed results.[2]

The treatment of SVT in children due to AV-nodal re-entry or bypass tracts whether manifest or concealed may be of particular interest to the anesthesiologist. Unfortunately, the use of vagal maneuvers in children is quite often ineffective to terminate SVT.[9] In infants, whether the SVT is due to AV-nodal re-entry or bypass tracts, there is usually a favorable response to digitalis.[9, 25, 33] The total digitalizing dose is 20 to 30 μg per kg in the premature and 40 to 50 μg per kg in the full-term infant. In the patient not previously on digitalis and who has normal electrolytes, 25 to 50 per cent of this dose may be given acutely. If digitalization is ineffective, propranolol or DC cardioversion may be effective.[33] Some authors would recommend the use of DC cardioversion before digitalization due to the increased likelihood of inducing ventricular fibrillation in the digitalized patient. However, DC cardioversion should not be withheld in a patient with severe hemodynamic compromise even if digitalized.

Wolff-Parkinson-White Syndrome

Wolff-Parkinson-White syndrome has long presented a therapeutic dilemma to both cardiologists and anesthesiologists (Fig. 5). In dealing with Wolff-Parkinson-White syndrome it is important for the anesthesiologist to realize that this is another situation where children are not "little adults" and respond differently to pharmacologic treatment than do adults. The use of digitalis in Wolff-Parkinson-White syndrome has long been a controversy since it is known to shorten the refractory period of bypass tracts in 50 per cent of adults[3] and potentially worsen SVT in patients with antegrade conduction (antidromic) via the bypass tract. Pediatric cardiologists have used digitalis in children for many years with an excellent safety record. This could possibly be due to the fact that most children exhibit orthodromic SVT; that is, antegrade conduction is via the AV node.[33] Propranolol is also an excellent drug to use since it also decreases AV conduction but has no effect on the accessory pathway. Quinidine and procainamide may also be effective, as they act on the accessory pathway and may interrupt the re-entry limb of the circuit.[33] Even though digitalis has been used safely in children, it should be avoided in cases where atrial fibrillation or flutter is present, as this may induce ventricular fibrillation due to increased conduction via the accessory tract.[33] It should also probably be avoided in wide QRS tachycardia, as antidromic conduction is more likely in this case and digitalis may worsen the arrhythmia. Quinidine or procainamide may be a better choice in this situation.[21] Ideally, patients with Wolff-Parkinson-White syndrome

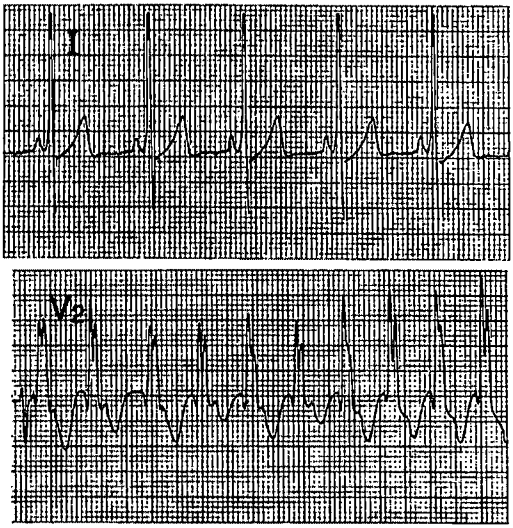

Figure 5. ECG from patients with Wolff-Parkinson-White syndrome showing delta wave and wide QRS tachycardia. (Tracings courtesy of Ed Colvin, MD, U.A.B. Department of Pediatric Cardiology.)

and SVT should undergo electrophysiologic study to document the effect of drugs on accessory conduction.[10] The anesthesiologist, however, should always be aware that DC cardioversion may be the most rapid and effective way of terminating SVT in the operating room and that pharmacologic measures may be used later in an attempt to maintain normal sinus rhythm.[34]

The anesthesiologist may be involved with intraoperative mapping and ablation of the aberrant tracts in these patients. In these cases, prior discussion with the cardiologist regarding perioperative antiarrhythmic therapy is very important so as to facilitate the mapping procedure but maintain patient safety.

Prolonged QT Syndrome

The prolonged QT syndrome is a rare abnormality that may affect a patient's anesthetic management. There are two distinct types of prolonged QT syndrome; congenital (LQTS) and acquired (ALQTS) (Fig. 6). The congenital form may be further subdivided into three distinct symptoms. Jervell and Lange Nielsen described a condition with prolonged QT, congenital neural deafness, and syncope or sudden death. This has also been referred to as the surdocardiac syndrome. The inheritance pattern is via an autosomal recessive gene. Romano and Ward described a similar condition without deafness that has an autosomal dominant inheritance pattern and is three times more common than the form associated with deafness. Another form with an autosomal dominant inheritance pattern is familial ventricular

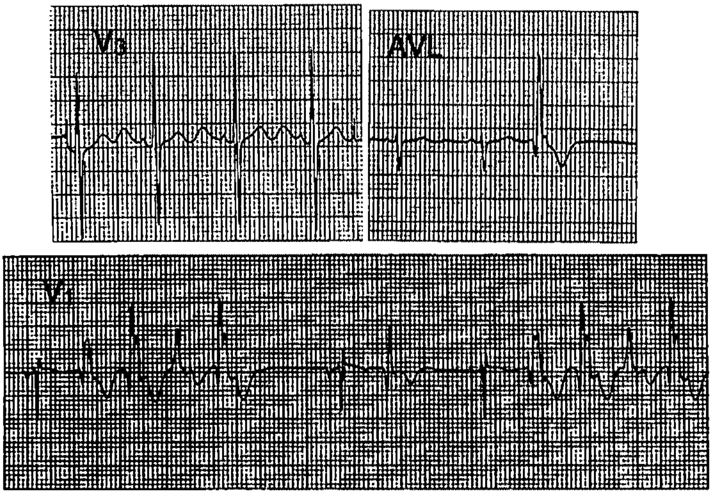

Figure 6. (*A*) ECG tracing of 10-year-old male with congenital prolonged QT syndrome (LQTS) without deafness. Note the markedly prolonged QT-U interval in lead V_3 and ventricular ectopy lead AVL. (*B*) ECG tracing of 6-year-old sister of preceding patient. Note the rare normally conducted beat and marked ventricular ectopy (lead V_1). (Tracings courtesy of Ed Colvin, MD, U.A.B. Department of Pediatric Cardiology.)

tachycardia, in which the QT is normal at rest but increases with exercise.[5, 13, 33] The acquired form has many causes and will be discussed later.

There are several theories that attempt to explain the underlying abnormality in LQTS but the most accepted theory is that of asymmetric sympathetic stimulation of the heart due either to decreased activity of the right cardiac sympathetic nerves or increased activity of the left nerves.[4, 5, 13, 27] The result of this imbalance may delay repolarization in some areas of the myocardium and predispose the patient to arrhythmias. These patients usually present with sinus rhythm but may exhibit numerous arrhythmias including bradycardia, atrial flutter, PVCs, bigeminy, or torsade de pointes.[5] There also may be alterations in the T waves with the T waves being prominent, broad, biphasic, or altering in polarity. U waves may also be present along with P waves superimposed on the T wave.[5]

These patients often have a history of syncopal attacks associated with sympathetic discharge. Symptoms may be precipitated by excitement, fright, fatigue, etc. Since sympathetic discharge seems to initiate symptoms in these patients, therapy has been directed at either blocking sympathetic discharge or by giving drugs that specifically shorten the QT interval. Beta-adrenergic blocking agents have by far been the most effective in decreasing mortality. Other agents that have been effective in patients who do not respond to beta blockade are phenytoin, digoxin, bretylium, verapamil, and phenobarbital. Left-stellate ganglion block has also been shown to be effective on a short-term basis or can be used to determine the effectiveness of left-stellate ganglionectomy for those patients who fail trials with pharmacologic agents.[4, 5]

The anesthetic management of patients with LQTS should be directed at minimizing sympathetic stimulation and use of those drugs that specifically decrease vagal tone or shorten the QT interval. These patients should receive beta blockers up to the time of surgery along with adequate sedation. Atropine is probably best avoided. The operating room should have a defibrillator, a transvenous pacemaker, drugs for treating cardiac arrhythmias, and means to monitor for air embolism if a stellate ganglionectomy is planned. During the operation, factors that cause sympathetic stimulation such as light anesthesia, hypoxia, hypocarbia or hypercarbia and hypothermia should be assiduously avoided. Thiopental has been the most commonly used induction agent and has not been implicated in causing serious arrhythmias. Ketamine, due to its ability to increase sympathetic discharge, may present problems. Muscle relaxants such as vecuronium or atracurium, with minimal effect on the autonomic nervous system, would seem to be indicated in this situation. Safe reversal of muscle relaxants can be achieved with neostigmine, atropine, or glycopyrolate.[5]

Maintenance agents may include nitrous oxide-oxygen, narcotics, or an inhalation agent. Halothane may be the least desirable inhalation agent due to its ability to sensitize the myocardium to catecholamines.

Isoflurane is probably the volatile anesthetic of choice due to its ability to shorten the QT interval and lack of sensitization of the myocardium to catecholamines. Since a Valsalva maneuver can prolong the QT interval, ventilatory patterns with high peak pressures or a high I to E ratio are best avoided.

Regional anesthesia may be used with caution as long as the patient is adequately sedated. Ideally, local anesthetic solutions are best prepared without epinephrine.

Extubation during "deep" anesthesia, and administration of a dose of lidocaine or a small dose of beta blocker before extubation, may be wise. Intensive care unit observation postoperatively will facilitate monitoring and treatment if required.

The acquired prolonged QT syndrome (ALQTS) is a syndrome separate from the congenital form and has numerous causes including myocarditis, myocardial ischemia, mitral valve prolapse, head injury, cervical surgery, adrenal insufficiency, amyloidosis, hypothermia, hypocalcemia, hypokalemia, hypomagnesemia, antiarrhythmic drugs, digoxin overdose, and others. It should be remembered that therapeutic interventions are also different for ALQTS. While beta blockers are the mainstay of treatment for LQTS and shorten the QT interval in these patients, they should not be used in patients with ALQTS as they prolong the QT interval in these as in normal patients.[5] Isoproterenol may, however, be a good therapeutic choice, as it shortens the QT interval in these patients, but it should not be used in LQTS.[5]

It has been noted that succinylcholine prolongs the QT interval in adults but that this is attenuated with pretreatment with d-tubocurarine.[5] It should also be noted that electrolyte disorders such as hypocalcemia, hypokalemia, and hypomagnesemia may prolong the QT interval and should be avoided in ALQTS.[5]

Ventricular Arrhythmias

Ventricular arrhythmias may occur in up to 2.8 per cent of the pediatric population.[14] As in adults, the form and frequency of the PVCs have a bearing on whether or not they should be considered benign or whether they are indicators of a serious condition. There is evidence to suggest that if PVCs are unifocal, disappear with exercise, or are in a bigeminal periodicity with a normal sinus beat interpolated, they are in fact benign.[14, 28] It has also been shown that in otherwise healthy infants, 95 per cent of PVCs disappear by 1 year of age.[29] Ventricular tachycardia is a more ominous, but less common, arrhythmia. It may be associated with drug toxicity from antiarrhythmic therapy, metabolic disturbances, intramyocardial tumors, mitral valve prolapse, IHSS, long QT syndrome, cardiomyopathy, or postoperatively after repair of congenital cardiac lesions. However, in 30 to 45 per cent of patients no underlying cause may be found and it is then classified as idiopathic. The incidence of sudden death varies with the underlying cause, with a range of 10 to 47 per cent, but is probably about 5 per cent in the idiopathic group.[4] Several of these causes may be of special concern to the anesthesiologist.

Ventricular arrhythmias have been found in 46 per cent of children with MVP, with 23 per cent of these arrhythmias considered serious. The incidence of sudden death has been reported between 1 and 2 per cent in adults and sudden death has been reported in children. The drug of choice for these arrhythmias is propranolol.[20, 28, 33]

Torsade de Pointes

Torsade de pointes is a special arrhythmia that may occur in children as well adults. It is characterized by a "twisting" of QRS peaks around the isoelectric line, with resultant "spindles" and "nodes." It is caused by an R-on-T phenomenon produced by prolongation of the QT interval. Marked bradycardia (for example, complete heart block) is the most common predisposing factor in addition to hypokalemia, and/or quinidine or procainamide therapy. Causes of prolonged QT, whether congenital or acquired, may result in torsade de pointes. There has also been an association with mitral valve prolapse.[6] Treatment of torsade de pointes is similar to that for any ventricular arrhythmia due to prolonged QT syndrome, and includes correction of any electrolyte abnormality and measures to accelerate the heart rate and thus shorten the QT interval: atropine and isoproterenol, but most important, atrial overdrive pacing.[6, 22]

Atrial Fibrillation and Flutter

Atrial fibrillation or flutter are relatively rare in the pediatric population unless the patient has congenital heart disease or has had an operation for congenital heart disease. Atrial fibrillation and flutter have been reported at approximately 5 per cent following repair of secundum ASD and may be as high as 10 to 36 per cent following transposition repair.[25] Other lesions associated with atrial fibrillation are Ebstein's anomaly, tricuspid atresia, cardiomyopathies, atrial tumors, and rheumatic heart disease.[33]

As mentioned previously, atrial fibrillation or flutter has been reported in utero and, if treated before 6 weeks postdelivery, the neonates generally do well.[33] Most symptoms in children are due to rapid ventricular response and rates of up to 300 beats per minute are not uncommon, especially if a bypass tract is present.[25, 33] Treatment is similar to that in adults. Digoxin is the most common pharmacologic treatment. It should be remembered, however, that digoxin may not be the treatment of choice when a bypass tract is known to be present. In that situation procainamide, propranolol, or quinidine may be effective.[25, 33] For the child in extremis with rapid ventricular responses, DC cardioversion with 1 to 2 W per second per kg may be used.[33] Also, if atrial pacing is available, overdrive pacing may be successful in terminating atrial flutter, but not fibrillation.[33]

Bundle Branch Block

Bundle branch block, whether left, right, or fascicular, is uncommon in the pediatric population unless it is accompanied by congenital heart defects or is in the patient who has undergone cardiac surgery. There have been families reported to have inherited right bundle branch block, left anterior fascicular block, and left bundle branch block.[13]

Isolated right bundle branch block is usually of no concern in the pediatric patient, even in the postoperative period. The right bundle is the most easily damaged intraoperatively but these patients seem to suffer few ill effects. However, when the patient reaches adulthood, he or she may develop complete AV block if left bundle branch block develops.[9]

Right bundle branch block with left anterior fascicular block is seen in patients with primum atrial septal defects and tricuspid atresia and probably represents abnormal development of the conduction system. The prognosis for patients who develop this postoperatively is not known.[9]

Left bundle branch block is rare in the pediatric population even postoperatively. Except in the patient who has undergone resection of a subaortic membrane, patients who develop left bundle branch block postoperatively should be considered for permanent pacing as they may have a greater risk for complete AV block.[9]

PREOPERATIVE AND INTRAOPERATIVE ARRHYTHMIAS

Preinduction anticholinergic medication is a common practice for many anesthesiologists who deal with children. This practice has fallen into disfavor in the adult population due to subjective discomfort and the possibility of inducing arrhythmias at induction. Due to the propensity of children to develop bradycardia during airway manipulation, anticholinergic premedication seems indicated in most cases. The most common arrhythmia at induction seems to be junctional rhythm or sinus bradycardia with nodal escape.[24] Atropine is useful in both instances. Atropine or scopolamine (0.01 to 0.02 mg per kg) intramuscularly or intravenously are probably the most common anticholinergics used in the pediatric population. Generally 0.1 mg is the lowest dose given, with 0.6 mg being the maximum. Dosage should be adjusted for the small preterm infant.[26] Atropine is a better vagolytic drug, with scopolamine having more amnesic properties. Both drugs cross the blood-brain barrier and may cause delirium.

Halothane is by far the most popular inhalation anesthetic agent used in the pediatric population. It is quite often used in children for inhalation induction due to the relatively good acceptance by the patient and lack of coughing and breath-holding. However, it has also been widely implicated in accentuating arrhythmias whether due to its direct depressant effect on cardiac conduction or its ability to sensitize the heart to catecholamines. By far the most common offending agents are the combination of halothane and succinylcholine, or possibly halothane and epinephrine. Also, elevated CO_2, hypoxia, and electrolyte imbalance are known to increase susceptibility to arrhythmias with halothane. Unfortunately, much of the data to date has been collected in adult subjects and extrapolation into the pediatric population may not be entirely valid.

Arrhythmias occur in 40 to 60 per cent of patients after receiving a single intravenous dose of succinylcholine.[26] The incidence varies with the anesthetic agent and the arrhythmias seem to be predominantly supraventricular.[26] Quite often sinus bradycardia or junctional rhythms predominate. As in adults, prior administration of intramuscular atropine seems to have little effect, but prior administration of intravenous atropine reduces the incidence and possible severity of these arrhythmias.[24, 26, 32] Interestingly enough, intramuscular succinylcholine does not seem to produce significant arrhythmias and may be related to the speed of absorption.[26] It has long been known that a second dose of intravenous succinylcholine may produce significant arrhythmias. The underlying mechanism for this is still in debate and may be due to "sensitization" of the myocardium to the second dose by the breakdown product of succinylcholine (succinylmonocholine).[26] Other authors suggest stimulation of the parasympathetic and sympathetic nervous systems.[35] Atropine may reduce the incidence of significant arrhythmias with multiple doses of succinylcholine.[35] Pentothal has been shown to have a significant protective effect, at least in adults, against succinylcholine-induced arrhythmias and possibly halothane-induced arrhythmias in general.[1, 30] This is possibly due to pentothal's action to inhibit enhanced vagal tone.[1]

The combination of halothane and epinephrine has long been known to have the potential to produce arrhythmias. Subcutaneously injected epinephrine is used extensively in the pediatric population to provide hemostasis, especially in ear, nose, and throat, and plastic surgery procedures. Interestingly enough, children seem to be surprisingly resistant to epinephrine-induced arrhythmias. The underlying mechanism for the arrhythmogenic potential for halothane-epinephrine interaction has not been fully elucidated, but increased blood pressure, increased heart rate, decrease in sinus and AV node automaticity, potassium release from the liver, or a direct effect by halothane on the myocardium have all been postulated.[7, 8, 19] It has been noted that the heart is "sensitized" with as little as 0.5 per cent halothane and that if arrhythmias do occur, deepening the anesthetic level with halothane has no effect on decreasing arrhythmias.[8]

The interaction of epinephrine with halogenated agents has been studied extensively in the adult population, with the recommended dose of epinephrine that does not produce arrhythmias being 1.8, 3.6, and 5.4 μg per kg for halothane, enflurane, and isoflurane, respectively.[8] There is also evidence that the addition of lidocaine to the infiltrate may be protective against arrhythmias and that the dose of epinephrine may be increased by as much as 50 per cent.[8, 16] Doses of up to 10 μg per kg with lidocaine have been used in normocarbic or hypocarbic children anesthetized with halothane, without the production of arrhythmias.[17] The reason for this is not clearly understood, but may be due to the fact that doses are based on weight as opposed to body surface area.[23]

If arrhythmias do occur in a child with an injection of epinephrine, ensure that the patient is adequately ventilated, is not hypoxic, and if possible, switch to another halogenated agent. Lidocaine or propranolol may be useful to suppress the arrhythmogenic response to the catecholamine stimulus. Another interesting point is that inasmuch as pentothal may have a protective effect in succinylcholine-induced arrhythmias, it may potentiate the arrhythmogenicity of halothane and epinephrine.[8] Etomidate does not seem to have this effect.[8]

As mentioned previously, hypoxia, hypercarbia, and electrolyte imbalance can all predispose the patient to intraoperative arrhythmias. Although not studied specifically in children, the threshold PCo_2 found to produce arrhythmias with halothane ranges between 60 to 140 torr with a mean of 92 torr.[18] The underlying mechanism for arrhythmias with both hypercarbia and hypoxia seems to be sympathetic activation and release of catecholamines.[18]

Electrolyte disorders are also a consideration in the differential diagnosis of intraoperative arrhythmias. Low potassium levels increase the rate of phase 4 depolarization, slow repolarization, and increase the transmembrane potential.[18] This predisposes to re-entry arrhythmias and to the discharge of automatic ectopic foci. High potassium levels slow conduction and decrease excitability of cardiac cells. If levels are high enough, this may produce asystole. Hypercalcemia is usually manifested by a prolonged QRS and PR interval with a shortened QT interval. Common arrhythmias associated with hypercalcemia are bradycardia and asystole.[18]

An arrhythmic stimulus that is seen frequently during strabismus surgery in children is the oculocardiac reflex. Its incidence ranges from 30 to 87 per cent and is seen more frequently with traction on the medial as opposed to the lateral rectus muscle.[18] The pathway consists of an afferent limb with fibers running with the long and short ciliary nerves to the ciliary ganglion and with the ophthalmic division of the trigeminal nerve to the ganglion. From the gasserian ganglion, fibers run to the main sensory nucleus of the trigeminal nerve with the efferent branch being the vagus.[18] Bradycardia and occasionally asystole are the usual arrhythmias seen. Retrobulbar block may lessen the incidence somewhat but this is poorly tolerated in young children. If arrhythmias occur, the surgeon should be notified immediately, traction released, and intravenous atropine given.

Transesophageal Electrocardiogram and Atrial Pacing

A recent advance in pediatric anesthesia is transesophageal ECG monitoring and atrial pacing (Fig. 7). The relative ease of intraoperative diagnosis and treatment of arrhythmias in children has been documented.[11, 12] Transesophageal ECG has been shown to be superior for P-wave detection as compared to surface ECG and may be very helpful in the intraoperative diagnosis of tachyarrhythmias where the P wave may be lost in the preceding T wave or be very low in

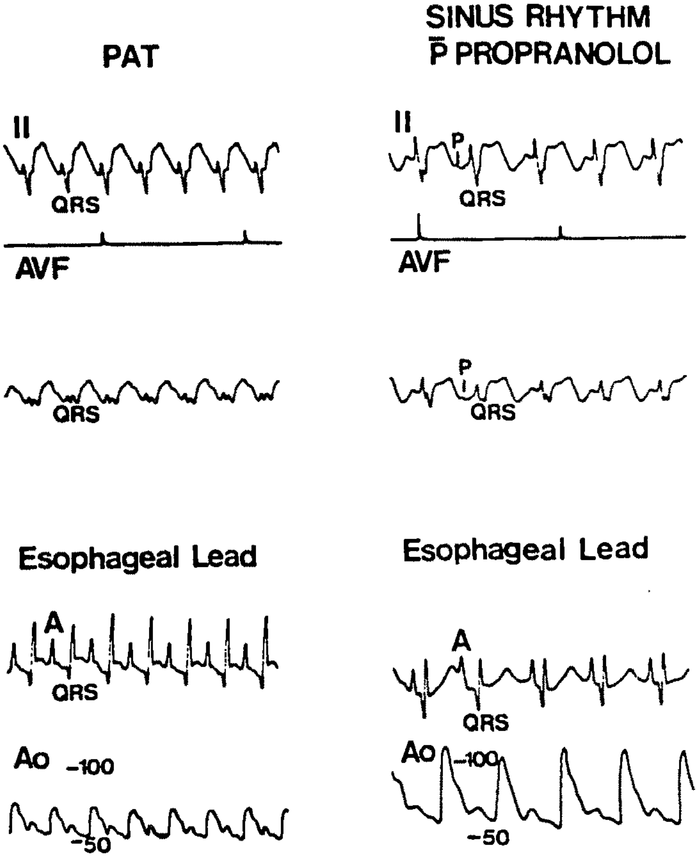

Figure 7. Intraoperative transesophageal and conventional ECG recordings with easily recognized atrial activity. (*From* Greeley WJ, Kates RA, Bushman GA, et al: Intraoperative esophageal electrocardiography for dysrhythmia analysis and therapy in pediatric cardiac surgical patients. Anesthesiology 65:669, 1986; with permission).

amplitude. Bipolar leads seem to be more effective in doing this. Transesophageal pacing has also been described for treatment of bradycardia and overdrive pacing for tachyarrhythmias. This method, using bipolar leads and atrial pacing when esophageal leads are placed such that the P wave is maximal, seems to be a rapid, noninvasive method for treatment of arrhythmias.[12] It is quicker and easier than emergency transvenous pacing in this pediatric population. It should be noted that only electrically isolated equipment should be used, and possibly the use of an electrocautery filter is indicated.[11, 12] Also, since neither ventricle lies close to the esophagus, only atrial pacing can be accomplished and treatment of AV block is not possible.[11]

SUMMARY

Arrhythmias do occur in the pediatric population and do not simply consist of sinus tachycardia and bradycardia. With more sophisticated monitoring, prenatal detection, and improved survival after cardiac surgery, the anesthesiologist can expect to see more children entering the operating room with the diagnosis of one form of arrhythmia or another. Some arrhythmias in pediatric patients may have a different significance than in adult patients. A complete knowledge of the arrhythmia, its history, implications, and associated disease entities, as well as different treatment modalities, is essential to providing a safe anesthetic for these pediatric patients.

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Diagnosis and Management of
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Pharmacologic Treatment of Arrhythmias

Laurie K. Davies, MD, and Richard F. Davis, MD†*

Drugs commonly used to treat arrhythmias have conventionally been classified into four major groups based on their electrophysiologic effects, as proposed by Vaughan Williams[100, 102, 109] (Table 1). Class I drugs, often referred to as "membrane stabilizers," interfere directly with depolarization. They may be subdivided according to their effects on action potential duration (APD) (Table 2): IA, prolongation of APD; IB, shortening of APD; and IC, little or no effect on APD. Class II drugs are beta-adrenergic antagonists. Class III drugs prolong repolarization and have marked antifibrillatory effects. Class IV drugs are often referred to as calcium antagonists and result in blockade of the slow inward depolarization current.

It should be recognized that this classification scheme, although useful, suffers several drawbacks. There may be considerable diversity within a class, noted especially in class I. A drug may possess electrophysiologic actions of more than one class. The drugs may also produce their in vivo effects not from direct electrophysiologic action but rather via indirect mechanisms, for example, activation or inhibition of autonomic function, reversal of ischemia, and improvement in hemodynamic function. Also, the choice of any antiarrhythmic is usually not based on its electrophysiologic profile. Rather, selection depends on the specific arrhythmia, the usual response of that rhythm to a particular drug, the patient's condition, and the urgency for treatment. Nevertheless, this classification system provides an excellent approach to the presentation, organization, and retrieval of the antiarrhythmic drugs.

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Table 1. *Classification of Antiarrhythmic Drugs*

EFFECT	I MEMBRANE STABILIZERS	II BETA-ADRENERGIC RECEPTOR ANTAGONISTS	III DRUGS PROLONGING REPOLARIZATION	IV CALCIUM ANTAGONISTS
Pharmacologic	Fast channel Na block	Beta-adrenergic block	Uncertain; possible interference with Na and Ca exchange	Decreased "slow-channel" calcium conductance
Electrophysiologic	Decreased rate of $\dot{V}$max	Decreased $\dot{V}$max; increased APD, ERP and ERP:APD ratio	Increased APD, ERP and ERP:APD ratio	Decreased slow-channel depolarization; decreased APD

Abbreviations: $\dot{V}$max, rapid depolarization; APD, action potential duration; ERP, effective refractory period.
From Davis RF: Etiology and treatment of perioperative cardiac dysrhythmias. *In* Kaplan JA: Cardiac Anesthesia, ed. 2. Philadelphia, Grune & Stratton, 1987; with permission.

CLASS I DRUGS

Quinidine

Electrophysiologic Effects. Quinidine's effects are a result of both direct action on the cell membrane and indirect (anticholinergic) effects. Quinidine decreases the slope of phase IV diastolic depolarization and increases the threshold potential.[45] This may result in suppressed automaticity in Purkinje fibers. A decrease in amplitude,

Table 2. *Subgrouping of Class I Antiarrhythmic Drugs*

	SUBGROUP		
	IA	IB	IC
Electrophysiologic activity			
Phase 0	Depressed	Slight effect	Marked depression
Depolarization	Prolonged	Slight effect	Slight effect
Conduction	Decreased	Slight effect	Marked decrease of velocity
ERP	Increased	Slight effect	Slight prolongation
APD	Increased	Decreased	Slight effect
ERP:APD ratio	Increased	Decreased	Slight effect
QRS duration	Increased	No effect during sinus rhythm	Marked increase
Prototype drugs	Quinidine, procainamide, disopyramide, diphenylhydantoin	Lidocaine, mexiletine, tocainide	Lorcainide, encainide, flecainide, aprinidine

Abbreviations: ERP, effective refractory period; APD, action potential duration.
From Davis RF: Etiology and treatment of perioperative cardiac dysrhythmias. *In* Kaplan JA (ed): Cardiac Anesthesia, ed 2. Philadelphia, Grune & Stratton, 1987; with permission.

in maximal rate of depolarization ($\dot{V}$max), and in overshoot of phase 0 of the action potential occur. These membrane effects are markedly decreased with hypokalemia.[110] Quinidine also demonstrates the property of "use-dependence,"[113] that is, a greater depressant action of quinidine is observed at faster heart rates. It is postulated that use-dependence results from a preferential interaction of the drug with either the open or inactive channel and very little from interaction with the resting channels of the unstimulated cell. With the decreased time spent in diastole at faster heart rates, the drug is distributed to a greater proportion of the receptors; therefore, the drug exerts more of an effect. The effective refractory period is markedly increased disproportionately to the duration of the action potential.

The effect on conduction through the atrioventricular (AV) node is unpredictable. Quinidine's direct effect is to prolong AV nodal and His Purkinje conduction times. However, quinidine may actually indirectly increase sinus rate and enhance AV nodal conduction because of its direct anticholinergic effect, as well as reflex sympathetic stimulation secondary to alpha-blockade-induced peripheral vasodilation.

Electrocardiogram. An increase in sinus rate may be observed. Prolongations of the QRS complex and of the QT interval occur, are concentration-dependent, and may be useful for monitoring therapy.

Hemodynamics. Quinidine markedly depresses myocardial contractility, especially if given rapidly intravenously. It also decreases systemic vascular resistance, primarily by alpha-adrenergic receptor blockade.

Clinical Application. Quinidine can be used to suppress atrial and ventricular arrhythmias. It also is used to maintain sinus rhythm after conversion of atrial flutter or fibrillation to sinus rhythm. However, most patients in atrial flutter or fibrillation should also be given digoxin or propranolol to slow ventricular response. If quinidine is used alone, it may slow the atrial flutter rate while at the same time enhancing AV nodal conduction and may result in a 1:1 AV conduction with dangerously high ventricular rates. Patients with Wolff-Parkinson-White syndrome and atrial flutter may be an exception to this rule because quinidine prolongs refractoriness and slows conduction in the accessory pathways mediating the ventricular response to atrial flutter.[114] Patients scheduled for elective direct-current (DC) cardioversion of atrial flutter or fibrillation often are given oral quinidine 1 to 2 days before anticipated cardioversion. About 10 to 20 per cent of patients will convert to normal sinus rhythm on this maintenance dose. Other patients will require cardioversion; maintenance quinidine therapy will help to prevent recurrence of atrial fibrillation.[87]

Quinidine may prevent recurrences of paroxysmal supraventricular tachycardia by prolonging atrial and ventricular refractoriness and slowing conduction in the retrograde fast pathway. It is generally contraindicated in digitalis-induced arrhythmias and in partial AV block because asystole may occur if progression to complete AV block occurs.

Side Effects and Drug Interactions. Quinidine has a low therapeutic ratio and side effects may contraindicate the long-term use of the drug in as many as 30 to 40 per cent of patients. Gastrointestinal (GI) intolerance is the most common problem during chronic oral therapy and may include diarrhea, anorexia, nausea, vomiting, and abdominal pain. Cinchonism may occur with large doses, which results in tinnitus, blurred vision, and headache, and GI and cardiac toxicity in advanced cases. "Quinidine syncope" may be a secondary ventricular tachyarrhythmia (torsades de pointes) and may not be dose-related.[98] Excessive prolongation of the QT interval (QT-c > 0.55 to 0.60) may indicate susceptibility to this complication. Rarely, hypersensitivity reactions to quinidine can cause fevers, rash, anaphylactic reactions, or thrombocytopenia. Quinidine may unmask or exacerbate myasthenia gravis.

Drugs that induce hepatic enzyme production (for example, phenobarbital, phenytoin, rifampin) may shorten the duration of quinidine's action by increasing its metabolism. Quinidine, on the other hand, will increase serum levels of digoxin, probably by releasing the glycoside from protein binding sites.[61] Quinidine may cause bleeding in patients receiving oral anticoagulants, although the mechanism is unclear.[57] Quinidine potentiates the action of nondepolarizing neuromuscular-blocking drugs.[74] Because quinidine has alpha-blocking properties, it can interact additively with drugs that cause vasodilation.

Dosage and Pharmacokinetics. Quinidine can be given either orally or parenterally, but the oral route is usually preferred because of the hemodynamic effects when given acutely intravenously. The usual oral dose is 200 to 600 mg every 6 hours. The sulfate form is absorbed rapidly; the gluconate form, more slowly. Bioavailability is about 60 to 80 per cent; and about 70 to 80 per cent of the drug is bound to plasma albumin. Recommended intravenous doses range from 0.1 to 0.2 mg per kg over 2 minutes, which can be repeated in 30 minutes if necessary.[7] Infusion rates of 0.005 mg per kg per minute have been used successfully. Blood pressure and electrocardiogram (ECG) must be monitored continuously when quinidine is administered intravenously. Intramuscular administration is generally not recommended because of pain on injection, increased creatinine phosphokinase, and unpredictable absorption. Quinidine is metabolized in the liver and excreted by the kidneys. Congestive heart failure, hepatic disease, and poor renal function decrease elimination of quinidine. Alkalinization of the urine can decrease renal excretion up to 50 per cent because quinidine is a weak base.

Procainamide

Electrophysiologic Effects. The electrophysiologic effects of procainamide (decreased Vmax and amplitude of phase 0, decreased rate of phase IV depolarization, and prolonged effective refractory period [ERP] over APD) are similar to those of quinidine. Procainamide slows conduction and increases ERP in atrial and His Purkinje portions of the conduction system, depressing both atrial and ventricular excitability. Minimal prolongation of AV-nodal conduction is observed. Anticholinergic effects occur, although this action is weaker than that of quinidine and disopyramide. AV-nodal ERP may decrease because of these indirect anticholinergic side effects. Local anesthetic potency of procainamide is greater than that of quinidine. Procainamide reduces differences in refractoriness between experimentally infarcted myocardium and normal myocardium.[77] Unlike many other class I drugs, procainamide's effects are less dependent on external potassium concentration.[92]

Electrocardiogram. ECG changes are similar to those seen during quinidine therapy. With therapeutic levels of procainamide, the QRS complex may be prolonged 5 to 10 per cent. The PR and QT intervals are also prolonged.

Hemodynamics. Procainamide causes direct myocardial depression at high plasma concentrations. It can also cause hypotension via peripheral vasodilation caused by ganglionic blockade. Alpha-adrenergic receptor blockade does not occur.

Clinical Applications. Similar to quinidine, procainamide has a broad spectrum of use. It is used to treat supraventricular and ventricular arrhythmias. Also like quinidine, procainamide is only moderately effective in converting atrial flutter or fibrillation to sinus rhythm but can be used to prevent recurrences of these rhythms after cardioversion. Pretreatment with digoxin, propranolol, or verapamil is indicated, however, to avoid an accelerated ventricular response. Both quinidine and procainamide are reported to reduce the frequency of short-coupling-interval (< 400 msec) premature ventricular contractions (PVCs) and, thus, reduce the frequency of ventricular tachycardia or fibrillation created by the R-on-T phenomenon.[59] Procainamide may be effective for reciprocating tachycardias in patients with Wolff-Parkinson-White syndrome by slowing conduction in the accessory pathways. In patients with digitalis toxicity, procainamide is best avoided because it may worsen AV block and may increase reentrant ventricular arrhythmias secondary to conduction delay.[123]

Side Effects and Drug Interactions. The high incidence of adverse reactions to procainamide, especially with chronic administration, limits its usefulness. One of the most troublesome side effects is the development of a lupus erythematosus-like (SLE) syndrome. In 50 to 70 per cent of patients taking the drug for 12 months, antinuclear antibodies develop; in about 30 per cent of these patients, clinical symptoms and signs of the SLE syndrome result if the drug is continued.[17] These manifestations may include arthralgias, fevers, hepatomegaly, pericarditis, and pericardial effusion. In this drug-induced syndrome, there is no predilection for females, and, generally, the brain and kidney are spared. The syndrome is reversible when the drug is discontinued.

Rapid intravenous injection of procainamide can cause severe hypotension and death.[105] High plasma concentrations of the drug may cause AV conduction disturbances and ventricular arrhythmias. Procainamide may worsen sinus node dysfunction in patients with sick sinus syndrome. Although procainamide prolongs the QT interval, torsade de pointes has only rarely been reported, as contrasted to its more frequent occurrence with quinidine therapy.[106] GI symptoms may occur but are less common than with quinidine. Hypersensitivity reactions (fever, rash, agranulocytosis, and nephrotic syndrome) occur occasionally.

Dosage and Pharmacokinetics. Procainamide can be administered orally, intramuscularly, or intravenously. Its relatively short half-life (3 to 4 hours) requires frequent oral dosing, although sustained-release preparations are also available. Total daily oral doses of about 3 to 6 g are usually required.

Procainamide should never be given rapidly intravenously because of its propensity to cause hypotension. One suggested method of administration is 100 mg (about 1.5 mg per kg) given over 2 to 4 minutes, with this dose repeated every 5 minutes until the arrhythmia is controlled, adverse effects occur, or a total dose of 1 g has been given. Arterial pressure and ECG must be carefully monitored during this therapy. Intravenous infusion rates for maintenance are 20 to 80 μg per kg per minute. The drug can also be given intramuscularly at a dose of 500 to 1000 mg every 4 to 8 hours.[118]

Procainamide depends on both the liver and kidney for its elimination. Hepatic metabolism is by acetylation and the major metabolite, N-acetyl procainamide (NAPA), has antiarrhythmic effects as well as toxic side effects. It is excreted almost entirely by the kidneys. The rate of acetylation is determined genetically and concentrations of both procainamide and NAPA in the plasma should be measured for optimal management.[121] Therapeutic levels of procainamide are 4 to 10 μg per ml and of NAPA, 2 to 22 μg per ml. At therapeutic concentrations, 15 per cent of the drug is bound to plasma proteins. Patients with impaired hepatic or renal function or with diminished perfusion of either organ, as in chronic heart failure, will show marked impairment in eliminating procainamide.

Disopyramide

Electrophysiologic Effects. Disopyramide is similar to quinidine and procainamide in its electrophysiologic effects. The amplitude and $\dot{V}$max of phase 0 are decreased, and there is a concentration-dependent decrease in the slope of phase IV depolarization. Repolarization is altered in experimental models, such that there is more homogeneous repolarization within infarcted and normal areas of myocardium.[94] Disopyramide prolongs the ERP more than the APD in normal Purkinje fibers and lengthens conduction time in normal and depolarized Purkinje fibers. Disopyramide is somewhat more potent than quinidine in increasing atrial or ventricular refractoriness and less potent in the His Purkinje system.

Disopyramide has greater anticholinergic effects than quinidine, and its atropine-like action nullifies some of its direct effects. Disopyramide may increase sinus rate and shorten AV-nodal conduction time and refractoriness by its vagolytic actions when the sinoatrial

(SA) and AV nodes are restrained by cholinergic influences. However, after cholinergic blockade, the drug substantially decreases sinus rate and increases SA node recovery time. Patients with conduction defects are prone to worsened block when disopyramide is administered. In patients with Wolff-Parkinson-White syndrome, disopyramide slows conduction time and lengthens the antegrade and retrograde refractory periods of the accessory pathways.[50]

Electrocardiogram. Disopyramide usually does not appreciably change sinus rate or the PR interval. At therapeutic concentrations, the QRS rarely widens by more than 20 per cent. The QT-c consistently lengthens by a small amount, and a prominent U wave may occur.

Hemodynamics. Disopyramide can markedly decrease myocardial contractility, with a reflex increase in systemic vascular resistance. Profound heart failure and hypotension may result in patients with left ventricular dysfunction. Adverse hemodynamic effects are more marked than those of quinidine, procainamide, lidocaine, or phenytoin. Chronic oral disopyramide therapy (200 mg every 6 hours for 1 week) has been shown to have a greater negative inotropic effect than chronic propranolol therapy (80 mg every 8 hours for 1 week).[23]

Clinical Application. Disopyramide is effective against ventricular and supraventricular arrhythmias. This drug reduces the frequency of PVCs in acute myocardial infarction, but its role in preventing death in this setting is not established. Disopyramide can be used to maintain sinus rhythm after conversion from atrial fibrillation as effectively as quinidine. However, like quinidine and procainamide, disopyramide may increase the ventricular rate in patients with atrial flutter or fibrillation unless they receive digitalis or propranolol first. It may prevent reciprocating tachycardias or may slow the ventricular rate during atrial flutter and atrial fibrillation in patients with Wolff-Parkinson-White syndrome.[50]

Side Effects and Drug Interactions. The most common side effects are due to the drug's anticholinergic properties (about $\frac{1}{10}$ that of atropine) and include dry mouth, blurred vision, constipation, and urinary retention. Acute angle glaucoma may be precipitated. Severe hypoglycemia has been reported. GI symptoms may occur but are less common than with quinidine. Ventricular tachycardia (of the torsade de pointes type) may occur with disopyramide, as with quinidine and procainamide, usually after marked QT prolongation. Disopyramide may precipitate or worsen heart block and may cause unacceptably high ventricular rates in patients with atrial fibrillation or flutter who have not received digoxin. Its potent negative inotropic and vasoconstrictive effects limit its usefulness because heart failure may be easily precipitated in patients with marginal reserve.[83]

Disopyramide, unlike quinidine, does not increase serum digoxin levels. Concomitant administration of phenytoin may decrease disopyramide levels by altering its metabolism. Disopyramide prolongs the duration of nondepolarizing neuromuscular blockade.

Dosage and Pharmacokinetics. The usual oral dose for adults is

100 to 200 mg every 6 hours.[56] The dose must be decreased in patients with renal or hepatic dysfunction and in patients with cardiac decompensation. When given orally, 80 per cent of disopyramide is absorbed. Its half-life is about 7 hours, with elimination by both hepatic and renal mechanisms. Protein binding is concentration-dependent, with about 30 to 50 per cent binding at therapeutic concentrations.

Lidocaine

Electrophysiologic Effects. The electrophysiologic effects of lidocaine are somewhat similar to quinidine in that there is a marked reduction in Vmax of atrial and ventricular potentials. Also, the slope of phase IV depolarization is reduced, which results in decreased automaticity in Purkinje fibers. However, like other class IB drugs, lidocaine decreases the APD in ventricular muscle and Purkinje tissue, such that the ratio of APD:ERP is less than 1. Lidocaine's effects are variable, depending on the potassium concentration and pH.[78, 103] In the normal heart, lidocaine has minimal effects on heart rate, automaticity, and conduction but may suppress SA node automaticity in patients with sinus node dysfunction. This drug may also suppress automaticity in junctional pacemakers during escape rhythms caused by ischemia. With impaired AV conduction, lidocaine can precipitate complete heart block, usually localized to the His Purkinje system, not the AV node. Lidocaine causes a decrease in ERP and the relative refractory period of the His Purkinje system but has no consistent effect on the ERP of the atria or the AV node. In some people, significant shortening of the ERP of the AV node may occur, which results in acceleration of the ventricular rate in atrial flutter.[2] Lidocaine has no important effects on the autonomic nervous system; most of its antiarrhythmic effects are caused by direct actions. Lidocaine increases the threshold for ventricular fibrillation.[37] It also decreases the disparity in the APD in normal and ischemic myocardial cells,[22] resulting in more uniform depolarization throughout the myocardium. This drug is most effective in hyperkalemic, acidotic myocardium, which may explain its effectiveness in the setting of myocardial infarction.

Electrocardiogram. Lidocaine causes little change in the ECG. The QRS interval is not prolonged; the QT-c interval may shorten slightly.

Hemodynamics. Lidocaine has very little hemodynamic effects at therapeutic concentrations in normal individuals. Transient depression of myocardial contractility may occur in patients with ventricular dysfunction.[96] Toxic concentrations may produce peripheral vasodilation and myocardial depression, which result in hypotension.

Clinical Application. Lidocaine is probably the most widely used antiarrhythmic drug and offers significant advantages perioperatively. It can be used intravenously with rapid onset and offset of effects when continuous infusion is terminated. Clinically significant adverse hemodynamic effects are rare. Lidocaine has both local and general anesthetic properties, in addition to its antiarrhythmic effects.

Unfortunately, its antiarrhythmic spectrum is rather narrow; it appears best suited for treatment of ventricular arrhythmias and is generally ineffective against the supraventricular variety. Lidocaine is effective against ventricular arrhythmias caused by acute myocardial infarction, cardiac surgery, and digitalis toxicity and is frequently used as prophylaxis for ventricular fibrillation following myocardial infarction.[65] Lidocaine should be avoided in atrial flutter because enhanced AV node conduction and slowing of the flutter rate may cause 1:1 AV conduction and unacceptably high rates.[2] In the setting of acute myocardial infarction lidocaine is the indicated treatment of PVCs that (1) occur more frequently than 5 per minute, (2) are closely coupled to the T wave, (3) originate in multiple foci (or have multiple ECG forms), or (4) appear in groups of two or more (ventricular tachycardia).[115]

Side Effects and Drug Interactions. The major toxic side effects of lidocaine are CNS-related and dose-dependent. These may include drowsiness, disorientation, hearing loss, and paresthesias, with seizures, coma, and respiratory depression at toxic concentrations. Local anesthetic-induced seizures do not produce permanent damage to the CNS as long as cardiovascular and respiratory complications of the seizure are prevented. Lidocaine may result in hypotension in patients with severely compromised ventricular function and may depress the sinus node, automaticity, and AV node conduction in patients with pre-existing conduction system disease.[42]

Beta-adrenergic antagonists can decrease lidocaine's clearance by decreasing hepatic blood flow.[79] Cimetidine also decreases lidocaine's clearance, which results in higher plasma concentrations of the drug.[55] There also appears to be a progressive reduction in clearance with prolonged infusion of lidocaine, although the mechanism is unclear.[62]

Dosage and Pharmacokinetics. Lidocaine is only used parenterally; there is extensive first-pass hepatic metabolism after oral administration. Therapeutic levels range from 1.5 to 5 μg per ml, with serious toxicity at about 9 μg per ml. It has a short duration of action because of rapid redistribution and metabolism. Therapy is usually begun with an intravenous bolus dose of 1 to 1.5 mg per kg, followed by an infusion rate of about 15 to 50 μg per kg per minute.[115] Often a repeat bolus of about 0.5 to 1 mg per kg is required about 5 to 30 minutes later, when arrhythmias may recur because of declining lidocaine concentration. In an emergency situation, lidocaine can be given intramuscularly at a dose of 4 to 5 mg per kg. Therapeutic plasma concentrations will be reached within about 15 minutes and maintained for about 90 minutes.[64]

About 70 per cent of lidocaine is bound to plasma proteins. Lidocaine is metabolized in the liver, and any situation that decreases hepatic blood flow or function, such as liver disease, anesthetics, shock, or congestive heart failure, will decrease lidocaine's clearance. The volume of distribution of lidocaine is also substantially reduced in patients with heart failure.

Diphenylhydantoin

Electrophysiologic Effects. Diphenylhydantoin (DPH), or phenytoin, is unique among class I drugs in that it possesses a potent central sympatholytic effect that decreases cardiac sympathetic efferent nerve activity.[38] Some of its antiarrhythmic actions may, therefore, be mediated neurally. DPH exhibits both class IA and IB characteristics. Its actions also depend on the potassium concentration, drug concentration, and state of the cardiac fiber. Like lidocaine, DPH shortens the APD more than the ERP and, thus, decreases the APD/ERP in Purkinje fibers. In normal Purkinje fibers, DPH may or may not slightly decrease V̇max and amplitude of phase 0. However, in cells partially depolarized from cold, hypoxia, or cardiac glycosides, DPH may cause these cells to repolarize by increasing potassium conductance.[14] This results in an increase in maximal diastolic potential, V̇max of phase 0, and conduction velocity. In atrial fibers depressed by ouabain, enhancement of rate of increase in phase 0 of the action potential occurs with DPH administration, which may relieve SA block. Repolarization in Purkinje fibers is accelerated. The slope of phase IV depolarization is moderately decreased, but automaticity is rarely abolished. No consistent effects on His Purkinje or AV-nodal conduction times have been found in normal subjects. The AV-nodal refractory period usually shortens significantly when DPH is given to patients receiving digoxin. Therapeutic concentrations of DPH have no effect on normal sinus node function. However, the sinus node may be depressed in patients with sinus node disease or with toxic concentrations of the drug. DPH is effective in abolishing triggered activity due to digitalis-induced delayed after-depolarizations in Purkinje fibers. This characteristic may explain its effectiveness in treating digitalis-induced arrhythmias. DPH has no peripheral cholinergic or beta-adrenergic blocking activity.

Electrocardiogram. DPH has little effect on the ECG. The PR interval may decrease slightly and there may be some shortening of the QT interval.

Hemodynamics. DPH is usually well tolerated although decreased contractile function and a moderate increase in left ventricular end-diastolic pressure (LVEDP) may occur.[66] These effects may be partially due to the solvents propylene glycol and ethyl alcohol used for the injectable preparation. Rapid intravenous administration (> 50 mg per minute) has produced cardiovascular collapse, ventricular fibrillation, and death.[108]

Clinical Application. DPH is generally considered a second-line drug and is rarely used alone. Currently, its main use is to control atrial and ventricular arrhythmias secondary to digitalis toxicity. It is variably effective against ventricular arrhythmias unrelated to digitalis. It has been reported to be moderately effective for ventricular arrhythmias following open heart surgery and those associated with general anesthesia[124]; however, most clinicians consider lidocaine a safer, more easily administered drug in those settings. DPH is ineffective against atrial arrhythmias and is uniformly *un*successful in converting atrial fibrillation or flutter to sinus rhythm. This drug is contraindicated in patients with severe bradycardia or high-grade AV block.

Side Effects and Drug Interactions. CNS symptoms including drowsiness, nystagmus, ataxia, diplopia, and vertigo are the major side effects. With severe overdosage, coma may ensue. The CNS effects are generally seen at plasma levels greater than 20 μg per ml. If these effects are seen, but the arrhythmia persists, DPH should probably be discontinued because the arrhythmia is unlikely to respond, even at higher plasma concentrations. Nausea, epigastric pain, and anorexia are relatively common. With chronic use, macrocytic anemia, gingival hyperplasia, pseudolymphoma, skin rashes, hirsutism, hyperglycemia, hypocalcemia, and peripheral neuropathy may occur. If administered too rapidly by the intravenous route, cardiac arrhythmias and hypotension may result.

An increase in the plasma concentration of DPH may occur with concomitant administration of coumadin, chloramphenicol, disulfiram, isoniazid, cimetidine, and certain sulfonamides. Other agents, which are also hydroxylated by the microsomal enzyme system, may inhibit DPH's hepatic inactivation and result in increased plasma concentrations. A decrease in phenytoin concentration is caused by carbamazepine, which enhances its metabolism. DPH increases the clearance of quinidine sulfate and theophylline. It enhances the metabolism of corticosteroids and may decrease the effectiveness of oral contraceptives.[86]

Dosage and Pharmacokinetics. DPH can be given either orally or intravenously. Intramuscular administration should be avoided because it has limited solubility at physiologic pH and may result in variable absorption, pain, and muscle necrosis. Variable absorption is also reported with oral administration and, because its clearance is affected by so many drugs, plasma levels may need to be monitored closely. Therapeutic plasma levels range from 10 to 20 μg per ml, with toxicity occurring at greater than 25 μg per ml. The oral dose in adults is generally 300 to 500 mg per day given in 1 to 4 divided doses. Intravenously, DPH is given in increments of 100 mg every 5 minutes to the desired effect, or to a total dose of 1000 mg, or until signs of toxicity (nystagmus) occur. When given intravenously, a large vein must be used to try to avoid phlebitis because the pH of dissolved DPH is so high (pH = 11.0). DPH should not be given at a faster rate than 25 to 50 mg per minute.

DPH is 70 to 90 per cent bound to plasma proteins. Elimination of DPH is primarily by hepatic metabolism, with only 5 per cent of unchanged DPH excreted by the kidneys. The dosage of DPH must be reduced in patients with severe liver disease. In some patients the enzyme system that metabolizes DPH becomes saturated with the drug, so that elimination becomes dose-dependent and unexpected toxicity results.

Tocainide

Electrophysiologic Effects. Tocainide's electrophysiologic effects are almost identical to those of lidocaine. Tocainide has membrane-stabilizing effects that decrease excitability of myocardial cells; however, it has no important effects on AV or intraventricular conduction. Tocainide decreases the effective refractory periods and APD.[84] It increases the ventricular fibrillation threshold in both normal and ischemic tissues. In contrast to lidocaine, tocainide prolongs the refractory period of the accessory pathway in patients with Wolff-Parkinson-White syndrome, but its efficacy for this condition has not been established.

Electrocardiogram. Tocainide generally has no important effects on ECG parameters. Some authors have reported a slight decrease in QT-c intervals.

Hemodynamics. Tocainide is usually tolerated quite well and has little hemodynamic effect. A modest negative inotropic effect may be seen, with the potential for exacerbating congestive heart failure.

Clinical Application. Tocainide is an amide analog of lidocaine, which was developed specifically for oral use. It is most effective in decreasing the frequency of PVCs. It has also been used for ventricular tachycardia but is rarely effective as a single agent for sustained ventricular tachyarrhythmias. Responsiveness to lidocaine often is predictive of therapeutic success with tocainide.[91] It may also be particularly indicated in patients with associated QT prolongation. It is ineffective for supraventricular arrhythmias.

Side Effects and Drug Interactions. Side effects are common and often result in discontinuation of the drug. These effects are dose-related and include nausea, vomiting, tremor, ataxia, light-headedness, paresthesias, and memory impairment. Hepatitis, convulsions, and a lupus-like syndrome may occur. Agranulocytosis and pulmonary fibrosis have also been reported. Tocainide may aggravate congestive heart failure and pre-existing AV-conduction disturbances. There is a potential for additive effects regarding myocardial contractility with concomitant beta-blocker therapy.

Dosage and Pharmacokinetics. Tocainide is generally given orally, although intravenous therapy has been used on an investigational basis.[40] Amide substitution prevents extensive first-pass hepatic metabolism, such that bioavailability approaches 100 per cent. About 40 per cent of the drug is excreted unchanged by the kidneys, and the dosage must be adjusted in patients with renal impairment. Metabolism is only slightly affected by chronic liver disease. Oral dosages of 800 to 2400 mg per day in 2 to 4 incremental doses are usually given. Plasma concentrations greater than 3 μg per ml are required for efficacy, while increasing side effects are seen at concentrations above 10 μg per ml.[120]

Mexiletine

Electrophysiologic Effects. Mexiletine hydrochloride is a class IB drug with electrophysiologic effects and chemical structure similar to lidocaine. It is a potent local anesthetic, which was originally developed as an anticonvulsant drug and was then found to have antiarrhythmic effects. Mexiletine reduces the V̇max of the action potential but has little effect on resting membrane potential or sinus node automaticity. A concentration-dependent reduction of APD occurs with mexiletine. Mexiletine may be more likely than lidocaine to further reduce conduction velocities in patients with impaired AV-nodal and ventricular conduction. Patients with sick sinus syndrome may suffer severe bradycardia with mexiletine administration.

Electrocardiogram. Mexiletine, at therapeutic concentrations, has no significant effects on ECG intervals.

Hemodynamics. Mexiletine has mild negative inotropic effects. Small decreases in contractility and increases in LVEDP have been noted but have been transient in almost all cases.[20, 95]

Clinical Applications. Mexiletine has been used effectively in reducing PVCs following myocardial infarction.[21] Variable success has been reported with therapy of recurrent ventricular tachycardia. In patients with serious ventricular tachyarrhythmias, it is rarely effective as a single agent, but combinations of mexiletine and other drugs may be effective and better tolerated.[52] It is not useful for supraventricular arrhythmias.

Side Effects and Drug Interactions. The most common side effects of mexiletine are CNS- and GI-related. Nausea and vomiting are frequent and may be alleviated somewhat by administering the drug with food. CNS effects include tremor, blurred vision, ataxia, drowsiness, memory impairment, changes in personality, insomnia, and, rarely, seizures. Occasionally, asymptomatic antinuclear antibody titer, rashes, and liver function abnormalities may develop. Cardiovascular toxicity may manifest as hypotension, sinus bradycardia, widened QRS, AV dissociation, and ventricular tachyarrhythmias, particularly with rapid intravenous injection. Mexiletine may precipitate supraventricular tachycardias in patients with Wolff-Parkinson-White syndrome.

When drugs that induce hepatic microsomal enzymes are given with mexiletene, decreased plasma levels will result. Cimetidine coadministration increases mexiletene levels. Alkalinization of urine will decrease renal clearance and may increase blood levels. Enhanced antiarrhythmic efficacy has been reported by combining mexiletene with beta-adrenergic blocking drugs or with quinidine.

Dosage and Pharmacokinetics. Mexiletine is well absorbed when given orally and is about 70 per cent protein-bound. Its metabolism is principally hepatic, 10 per cent of the drug being excreted unchanged in the urine. Therapeutic levels range from 0.75 to 2 μg per ml, and side effects are likely when levels exceed 2 μg per ml. The usual oral dosage is 200 to 400 mg every 8 hours.

Encainide

Electrophysiologic Effects. Encainide markedly depresses V̇max by depressing the fast sodium current (with a very long time constant to recovery), which decreases conduction velocity in Purkinje fibers. It has little effect on the APD or the ERP, which characterizes the drug as belonging to class IC. Encainide depresses spontaneous phase IV depolarization and suppresses various types of abnormal automaticity. Electrophysiologic effects differ when the drug is given orally or intravenously, which suggests that it possesses active metabolites with different antiarrhythmic actions.[71] When given intravenously, encainide slows conduction in the His Purkinje system, without greatly affecting conduction or refractoriness in other parts of the conduction system. However, orally, it increases refractoriness in the atria, ventricles, and accessory pathways and depresses AV-nodal conduction. It also can elevate the ventricular fibrillation threshold.

Electrocardiogram. Encainide prolongs the PR and QRS intervals, but the QT interval increases only to the extent that the QRS lengthens. A marked effect on the QRS interval is one indication to decrease dosage.

Hemodynamics. Mild negative inotropic effects have been demonstrated, although hemodynamic effects are slight, even with left ventricular dysfunction.[27]

Clinical Application. Encainide is effective for both supraventricular and ventricular arrhythmias. Total or near abolition of ventricular ectopy has been reported in 44 to 90 per cent of patients given the drug on a short-term basis.[1, 30, 119] Encainide controls refractory ventricular tachyarrhythmias in about 50 per cent of patients during 6 months of therapy, but its effectiveness decreases to about 25 to 30 per cent over a longer period of time. It is useful in treating supraventricular tachyarrhythmias caused by AV-nodal re-entry, which includes reciprocating tachycardia in patients with Wolff-Parkinson-White syndrome.[1]

Side Effects and Drug Interactions. Adverse side effects include neurologic or GI disturbances manifested by dizziness, nausea, vomiting, headaches, tremors, diplopia, and syncope. More importantly, encainide may cause or exacerbate arrhythmias, particularly in patients with poor ventricular function, conduction disease, or a history of sustained ventricular tachyarrhythmias.[31] Polymorphic ventricular tachycardias without QT prolongation have been reported with a frequency of about 10 per cent in patients with histories of ventricular tachycardia or ventricular fibrillation. Encainide may make the conversion of ventricular tachyarrhythmias to sinus rhythm more difficult and may increase the pacing threshold.

Interactions with other cardiac drugs are possible, although no significant interactions have been observed with digoxin, warfarin, beta-blockers, or calcium channel-blockers.[85] Cimetidine increases the plasma concentration of encainide and its metabolites, but the clinical effect of this interaction is unclear.

Dosages and Pharmacokinetics. Encainide absorption is variable, with a wide range of clearances resulting in an unpredictable range of plasma levels. There are two active metabolites that may account for a great deal of effects seen during chronic therapy. Metabolism is affected in patients with hepatic dysfunction but the clinical importance of this is unclear because there is no simple relationship between drug levels and efficacy. In moderate-to-severe renal impairment, dosage must be reduced. Usual oral doses range from 75 to 225 mg per day in 3 to 4 incremental doses.[6]

Flecainide

Flecainide acetate is a derivative of procainamide with predominant class IC activity. It depresses phase 0 and slows conduction throughout the heart; delays repolarization in canine ventricular muscle; and increases intracardiac monophasic APD. Thus, this drug has both class IC and class III properties.[80] Flecainide may depress sinus node function, particularly in patients with intrinsic sinus node disease. Pacing threshold is increased and flecainide should be used cautiously in patients with artificial cardiac pacemakers.

Electrocardiogram. Flecainide prolongs PR, QRS, and QT-c intervals in a dose-related fashion.

Hemodynamics. Flecainide has negative inotropic effects, but oral flecainide is usually well tolerated as measured by arterial pressure, echocardiographic parameters, and exercise tolerance.[4, 88]

Clinical Application. Flecainide is very effective in suppressing both ventricular and atrial arrhythmias. It is most effective in suppressing ventricular arrhythmias in patients with good ventricular function, no history of sustained ventricular tachyarrhythmias and absence of conduction system disease. It may actually be proarrhythmic in compromised patients with recurrent ventricular arrhythmias. Flecainide may be effective in decreasing rapid AV and ventricular-atrial conduction, particularly in patients with accessory pathways. The drug has recently been used for various supraventricular arrhythmias, with some success in conversion of atrial fibrillation to sinus rhythm.[18]

Side Effects and Drug Interactions. Side effects have been reported in about 30 per cent of patients and these include dizziness, blurred vision, headache, nausea, tremor, and diarrhea. High-degree AV block may occur in patients with pre-existing bundle branch block. QT prolongation with induction of polymorphic ventricular tachycardia has been reported.[69] Exacerbation of congestive heart failure may occur with intravenous administration or initial loading with large oral doses.

Flecainide minimally increases digoxin levels, and both flecainide and propranolol levels increase with the coadministration of the two drugs. Caution should be used if other class I antiarrhythmics are concomitantly administered.

Dosage and Pharmacokinetics. Flecainide is well absorbed orally and has a long plasma half-life, permitting twice daily dosing, a distinct advantage over other antiarrhythmics. It is 40 per cent protein-bound, and about 30 per cent is excreted in the urine unchanged. Several days are necessary before a steady state is achieved. Its rate of elimination is decreased in patients with congestive heart failure or renal insufficiency. Therapeutic plasma levels are usually in the

0.2 to 1.0 μg per ml range. Typical doses range from 100 to 300 mg orally twice a day. On an investigational basis, it has been used intravenously in doses up to 2 mg per kg over 20 minutes, particularly for control of rapid ventricular rates in Wolff-Parkinson-White syndrome.[80]

CLASS II DRUGS

Class II agents produce their antiarrhythmic effects by competitive blockade of beta-adrenergic receptors. Beta-blockers have many diverse, therapeutic uses. These drugs all have the same antiarrhythmic potential, and selection of a beta-blocker is generally made according to properties that reduce adverse effects or that affect dosing intervals or drug interactions. Propranolol is the prototype of this class.

Propranolol

Electrophysiologic Effects. Most of propranolol's antiarrhythmic effects probably result from its beta-adrenergic blocking action, which decreases the rate of spontaneous phase 4 depolarization in the SA node, the magnitude of which depends on background sympathetic tone. Propranolol has little effect on sinus rate when catecholamines are absent. The inhibition of the increase in heart rate in response to exercise or stress is marked. Propranolol also depresses automaticity in the AV node and more distal portions of the conduction system. Under normal conditions, the threshold for ventricular fibrillation is not consistently increased, but the drug does increase the threshold for fibrillation after experimental infarction.[35] Propranolol does not appreciably affect the APD in the sinus node, atrium, or AV node. In ventricular muscle, APD shortens slightly, and in Purkinje fibers, APD often shortens substantially. Propranolol increases the ERP of the AV node, which is most commonly the basis for its efficacy in the treatment of most tachyarrhythmias. It has little effect on ERP of normal atrial or ventricular muscle.

In addition to beta-blockade, propranolol also possesses two properties that may be important to its antiarrhythmic effect. Propranolol decreases the background outward current of potassium and, at higher concentrations, also inhibits inward sodium current. These effects are similar to class I effects and have been termed membrane-stabilizing activity, or quinidine-like effects. This local anesthetic action results in a reduction of the Vmax of the action potential and a reduction in the overshoot potential. At high concentrations of propranolol, membrane responsiveness and conduction are depressed in normal atrial and ventricular muscle and Purkinje fibers. There is considerable controversy over this issue, but most authors feel that propranolol's membrane-depressant effects are not responsible for its antiarrhythmic efficacy, because membrane-stabilizing activity occurs only at levels about ten times greater than those necessary to produce beta-blockade.[25] Most of the drug's antiarrhythmic actions can be explained on the basis of beta-blockade, although, occasionally, very high concentrations are required to control ventricular arrhythmias.[122]

The antiarrhythmic effect of propranolol may be multifactorial. AV-nodal re-entry often causes paroxysmal supraventricular tachycardia and, in such cases, the increased AV-nodal ERP caused by beta-blockade may abolish the re-entry. At the ventricular level, propranolol abolishes catecholamine-induced after-potentials and decreases Purkinje fiber response by means of membrane-stabilizing activity. Myocardial metabolic effects of beta-blockade may be indirectly antiarrhythmic by decreasing the severity of ischemia.

Electrocardiogram. The PR interval may be prolonged and the QT-c slightly shortened, without any effect on the QRS complex. The degree of slowing of the sinus rate depends on the individual's intrinsic sympathetic tone.

Hemodynamics. Propranolol has significant negative inotropic effects and may worsen or precipitate heart failure. A significant increase in LVEDP has been observed and peripheral resistance usually increases, probably as a reflex mechanism.

Clinical Application. Propranolol is generally more useful in the therapy of supraventricular than ventricular arrhythmias. It may terminate acute re-entrant supraventricular tachyarrhythmias that involve the SA or AV node in the re-entrant circuit. It slows the ventricular response in atrial fibrillation but rarely effects conversion to sinus rhythm. Combination therapy with quinidine or procainamide probably improves the likelihood of converting atrial fibrillation to sinus rhythm. Propranolol may be effective for treatment of some digitalis-induced arrhythmias, although dilantin or lidocaine are still preferable, especially if partial AV block is present. Propranolol can decrease the rate of sinus tachycardia caused by excess sympathetic stimulation. It may suppress PVCs and ventricular tachycardia, especially if exercise-induced. Propranolol may be useful in the treatment of ventricular arrhythmias associated with long QT syndrome or mitral valve prolapse syndromes. Beta-blockade may be especially useful in the perioperative setting in cases of hyperthyroidism, resection of pheochromocytoma, interaction of catecholamines with anesthetics, stress under light anesthesia, and high levels of anxiety. A reduction in the incidence of overall and sudden death has been reported in patients receiving beta-blockers in the year after experiencing acute myocardial infarction.[12]

Side Effects and Drug Interactions. Cardiac toxicity includes precipitation of congestive heart failure and impaired AV conduction. Hypotension and excessive bradycardia may occur in patients dependent on sympathetic stimulation for cardiac output. Complete heart block and asystole have occurred in patients with pre-existing AV-nodal or intraventricular conduction abnormalities. Bronchoconstriction can occur from beta-$_2$ receptor blockade, which may cause severe pulmonary compromise in susceptible patients. There is an increased risk of hypoglycemia because the sympathomimetic effects of hypoglycemia are blocked by propranolol. Other adverse effects include intermittent claudication, Raynaud's phenomenon, disturbed sleep, depression, impotency, and easy fatigability. Sudden withdrawal of beta-blockade therapy may worsen angina or precipitate cardiac arrhythmias or acute myocardial infarction.[73]

Dosage and Pharmacokinetics. Absorption of propranolol is excellent but bioavailability is only about 30 per cent owing to extensive first-pass hepatic metabolism. Reduction in hepatic blood flow significantly decreases hepatic metabolism and increases plasma levels of the drug. Also, in patients with marginal cardiac reserve, propranolol will further reduce its own elimination by reducing cardiac output and hepatic blood flow. Propranolol is 90 to 95 per cent protein-bound, with an elimination half-life of about 3 to 4 hours. The duration of action can be prolonged by administering large doses because propranolol has a greater margin of safety than many other antiarrhythmic drugs.

Effective propranolol dosage is variable and is determined by therapeutic response. The usual oral dose is 40 to 400 mg per day, divided into four doses. Resistant arrhythmias may require 1000 mg per day. The adult intravenous dose is 0.25 to 1.0 mg administered every 5 minutes until the desired effect or signs of toxicity or to a total dose of 0.15 to 0.20 mg per kg. Stable therapeutic plasma concentrations of propranolol can be achieved with continuous intravenous infusion of about 3 mg per hour in adult postoperative patients previously receiving chronic treatment.

Esmolol

Esmolol is an ultra-short-acting, cardioselective beta-blocker. It has no significant intrinsic sympathomimetic activity or membrane-stabilizing properties. Its electrophysiologic properties are those typical of beta-blockade (vide supra). Its ECG effects are no different from those seen with propranolol. Its major advantage perioperatively is its extremely short half-life (about 9 minutes).

Hemodynamics. Intravenous infusions of esmolol decrease heart rate, cardiac output, contractility, and blood pressure in a dose-dependent manner. These effects can be expected to dissipate within 20 to 30 minutes after discontinuation of the infusion because of the drug's short half-life. Esmolol has no demonstrable alpha-adrenergic receptor effects.

Clinical Applications. Esmolol is used primarily for acute intravenous treatment of sinus or supraventricular tachycardia. In one multi-center, double-blind, randomized study of patients with supraventricular arrhythmias, esmolol decreased ventricular rate at least 20 per cent in 72 per cent of patients, compared with 69 per cent of patients given propranolol.[75] Conversion to sinus rhythm occurred in 14 per cent of these patients, compared with 16 per cent of propranolol-treated patients. Thus, esmolol is at least as effective as propranolol in patients with supraventricular arrhythmias and has the added advantage of cardioselectivity and short half-life. Other studies have shown esmolol to compare favorably with verapamil and digoxin for recent-onset atrial fibrillation or flutter, with a significantly greater conversion rate to sinus rhythm and control of the ventricular response on a short-term basis.[82]

Esmolol is particularly well suited for control of perioperative supraventricular tachyarrhythmias, sinus tachycardia, and hypertension. Its short half-life provides an element of safety in treating critically ill patients under changing clinical conditions. It has also been used successfully for treatment of acute myocardial ischemia.[51] Its role in limiting infarct size is under investigation,[99] but esmolol clearly reduces the heart rate of patients with ischemia.

Side Effects and Drug Interactions. The most common side effect is transient hypotension; it most often is asymptomatic and resolves with a decrease or termination of infusion. Other adverse reactions are typical of beta-blockers and may include increased heart failure, dyspnea, claudication, bradycardia, nausea, vomiting, headache, and irritation at the infusion site.[75] Esmolol may potentially cause bronchospasm at high doses in spite of its cardioselectivity. Esmolol may cause phlebitis in concentrations greater than 10 mg per ml.

Esmolol should be administered cautiously to patients prone to bradycardia, heart block, hypotension, cardiac depression, or to those receiving drugs that potentiate these effects. No metabolic interactions between esmolol and other ester molecules are known. Specifically, esmolol doses up to 500 μg per kg per minute have not modified neuromuscular effects of succinylcholine.[39]

Dosage and Pharmacokinetics. Esmolol is infused at 20 to 200 μg per kg per minute. Increases in maintenance infusion may be preceded by loading doses of 100 to 500 μg per kg over 1 minute. The lower doses should be used in unstable, critically ill patients. Most responders require a dose of 150 μg per kg per minute or less.

Esmolol is rapidly metabolized ($t\frac{1}{2}$ = 9 minutes) by hydrolysis of its methyl-ester linkage. It is not affected by plasma cholinesterase; the esterase responsible for its metabolism is located in erythrocytes and is not inhibited by cholinesterase inhibitors, such as neostigmine, physostigmine, or edrophonium. Methanol and a primary acid metabolite are the by-products of metabolism, but methanol levels apparently are insufficient to cause toxicity, even with prolonged infusion. The acid metabolite possesses a slight degree (1500 times less than esmolol) of beta antagonism.[39]

CLASS III DRUGS

Bretylium

Class III drugs are distinguished by their prominent antifibrillatory effects, as opposed to antiectopic effects. However, only bretylium is marketed specifically for that purpose.

Electrophysiologic Effects. Bretylium exerts both a direct effect on cell membranes and an antiadrenergic action. The major direct effect is to prolong the APD and ERP of Purkinje and ventricular muscle fibers. This drug reduces the disparity in APD and ERP duration between regions of normal and infarcted canine myocardium,[33, 68] which may explain its prominent antifibrillatory effects. Bretylium fails to depress automaticity significantly; in fact, Purkinje fiber automaticity has been increased in experimental preparations,[15] but this effect is most likely due to release of catecholamines from adrenergic nerve terminals and has been abolished by pretreatment with either reserpine or propranolol.

Bretylium has marked antiadrenergic actions, but the cardiac response is biphasic after acute intravenous administration. Bretylium is taken up and concentrated in adrenergic nerve terminals and, initially, norepinephrine is displaced from these sites. With this release of norepinephrine, sympathomimetic effects may be seen, with increases in arterial pressure, vascular resistance, and cardiac automaticity. Initial catecholamine release may exacerbate some arrhythmias. After 20 to 30 minutes, this response wanes and the adrenergic blocking effects of bretylium predominate. Bretylium blocks the release of norepinephrine associated with nerve stimulation and also inhibits the uptake of norepinephrine and epinephrine into adrenergic nerve endings. Consequently, the actions of circulating catecholamines can be potentiated by bretylium. The antiarrhythmic effect does not depend on uptake of bretylium by adrenergic neurons, as evidenced by continued antiarrhythmic efficacy, even after treatment with tricyclic antidepressant drugs, which inhibit bretylium uptake into the neurons. The antiarrhythmic effect is also unaffected by cardiac denervation or by chronic reserpine therapy.

Bretylium has no significant effect on membrane responsiveness or conduction. It significantly increases the ventricular fibrillation threshold and may spontaneously convert ventricular fibrillation to sinus rhythm. Bretylium also decreases the amount of electrical current required to produce defibrillation.[107]

Electrocardiogram. In humans, bretylium decreases the sinus rate and increases the PR and QT intervals. The duration of the QRS complex does not increase. After acute intravenous administration, heart rate may increase.

Hemodynamics. Even high concentrations of bretylium do not impair myocardial contractility. In fact, an increase in contractility with an acute increase in blood pressure and heart rate may occur initially because of norepinephrine release. Subsequently, hypotension and bradycardia may develop because of the neuronal blocking action. Hypotension is particularly likely to occur with standing, as a result of blockade of the efferent limb of the baroreceptor reflex.

Clinical Application. Currently, bretylium is recommended only as a second-line drug for recurrent ventricular tachycardia and ventricular fibrillation. This class III drug is used when conventional, first-line drugs such as lidocaine, quinidine, and procainamide have failed. The antifibrillatory effect may require some time to develop, so full resuscitative efforts should be continued for at least 20 to 30 minutes after bretylium has been administered. The response of severe refractory ventricular arrhythmias has been impressive; bretylium may terminate such arrhythmias, facilitate DC cardioversion, and prevent recurrence. Bretylium should probably be avoided when arrhythmias are caused by excess digitalis and myocardial infarction because such arrhythmias may be aggravated by cathecholamine release.

Side Effects and Drug Interactions. The most common side effect is postural hypotension (with an incidence up to 66 per cent), but blood pressure may become unstable even in supine patients. Vasodilators or diuretics may intensify the hypotension. Acute administration may initially cause ventricular ectopy and hypertension; this may be intensified by concomitant vasopressor therapy. Nausea and vomiting may occur in conscious patients, particularly if the drug is given rapidly. Parotid pain has been reported with chronic oral therapy. Other less common adverse effects include bradycardia, precipitation of anginal attacks, diarrhea, abdominal pain, hiccups, rash, flushing, fever, sweating, nasal congestion, and mild conjunctivitis.

Dosage and Pharmacokinetics. In the United States, bretylium is approved only for parenteral use. It is eliminated entirely by renal excretion of the unchanged drug and dosage must be appropriately adjusted for patients with renal insufficiency. In treating ventricular fibrillation and ventricular tachyarrhythmias, bretylium is generally given as a bolus dose of 5 to 10 mg per kg, which can then be repeated as necessary to a total dose of 30 mg per kg if arrhythmias persist. Continuous infusion of 1 to 2 mg per minute may be used to maintain plasma levels. Onset of action after intravenous administration occurs within several minutes, but full antiarrhythmic effects may require 30 minutes to 2 hours. The average elimination half-life is about 9 hours.

Amiodarone

Electrophysiologic Effects. Amiodarone is structurally related to thyroxine and has antiadrenergic and antianginal properties, as well as antiarrhythmic actions. Its electrophysiologic effects are complex and differ for acute intravenous and chronic oral therapy. The major electrophysiologic action of this class III drug is to prolong both atrial and ventricular APDs. Given acutely intravenously, the drug slightly increases the ERP of the His Purkinje system and ventricular myocardium. Although AV-nodal ERP increases with acute intravenous amiodarone therapy, the increase is greater following chronic use. In other cardiac tissue, there is little or no change in ERP following intravenous administration; however, after chronic oral use, ERP is increased globally and AV conduction times are increased clinically.[125]

Amiodarone depresses sinus node automaticity and slows conduction through the AV node and specialized conduction system, but not in atrial or ventricular muscles. In most patients with Wolff-Parkinson-White syndrome, amiodarone increases the refractory period of the accessory pathway. Amiodarone increases the amount of electrical current required to elicit ventricular fibrillation (an increase in ventricular fibrillation threshold). It has been suggested that amiodarone is effective in suppressing ventricular tachycardia by a selective action on diseased cardiac tissue that lengthens the refractory period and slows conduction in a fashion similar to that of lidocaine.[43] Amiodarone also exhibits a noncompetitive alpha- and beta-adrenergic receptor antagonism, but the contribution of this effect to the antiarrhythmic action of the drug is not known.

The electrophysiologic effects of chronic amiodarone treatment seem to mimic those of thyroid ablation.[101] Moreover, the repolarization effects of the drug are reversed by tri-iodothryonine (T_3) administration. This suggests that among the basic effects of amiodarone is the blockade of the cardiac effect of T_3. This mechanism has been proposed as an alternative to the active metabolite-accumulation theory to account for the slow onset of amiodarone's antiarrhythmic effect.

Electrocardiogram. The QT-c is not prolonged by acute intravenous administration of amiodarone, but chronic oral ingestion significantly increases QT-c. Bradycardia and AV block may occur.

Hemodynamics. Amiodarone, a powerful coronary and systemic vasodilator with moderate noncompetitive alpha- and beta-receptor antagonism, does not cause clinically significant myocardial depression in patients with normal ventricular function. However, the drug may aggravate existing heart failure by its nonspecific adrenergic antagonism in patients in whom cardiac compensation is critically dependent on augmented sympathetic drive. Bradycardia and hypotension may occur. Cardiac output is usually well maintained or may even improve because of the marked decrease in left ventricular afterload.[26]

Clinical Applications Because of its serious toxicity, amiodarone is usually reserved for those patients who are unresponsive to other agents. It is effective for both atrial and ventricular arrhythmias. Even though it prolongs the QT-c interval, it may suppress recurrent ventricular tachyarrhythmias in patients with prolonged QT syndrome. Amiodarone is very effective in preventing recurrent paroxysmal supraventricular tachyarrhythmias, which may occur with the Wolff-Parkinson-White syndrome. This class III drug may be useful alone or in combination with other drugs to prevent recurrences of ventricular tachycardia or fibrillation in patients resuscitated from sudden death. Amiodarone also has been used to control episodes of tachycardia in patients with the sick sinus syndrome, but, because it may worsen bradycardia, a permanent pacemaker may be required.

Side Effects and Drug Interactions. Adverse effects occur commonly and can be fatal. The most common side effect is asymptomatic iodine-containing microdeposits of the drug throughout the body, but most readily noted in the cornea. These corneal microdeposits generally do not interfere with vision, although some patients may complain of blurring, halos, or other visual impairment with prolonged use of the drug. These usually resolve following discontinuation of the drug. Abnormal thyroid function tests (either hypothyroidism or hyperthyroidism) develop in about 2 to 4 per cent of patients.[3] Patients with pre-existing thyroid dysfunction seem more likely to suffer this problem, although the exact mechanism is unclear. Amiodarone contains 75 mg of iodine in each 200-mg dose.

A bluish skin discoloration and photosensitivity (57 per cent incidence) are annoying side effects, which are reversible with discontinuation of the drug.[44] Asymptomatic transaminase elevations are not uncommon, but clinical hepatitis is rare. The most serious noncardiac effect is pulmonary fibrosis, which can occur in up to 7 per cent of patients and may be fatal in 20 to 25 per cent of those affected.[90] Nausea, hair loss, insomnia, tremor, paresthesia, proximal muscle weakness, and ataxia have been reported. Cardiac side effects observed include prolongation of the QT interval, AV block resistant to atropine, sinus pauses, fatal cardiogenic shock, and proarrhythmic effects including torsades de pointes. Antiadrenergic effects of amiodarone may be enhanced in the presence of general anesthesia. Drugs that inhibit the automaticity of the SA node, such as halothane and lidocaine, could be additive and increase the likelihood of sinus arrest. In two case reports of anesthetized patients, bradycardia and hypotension were prominent.[19, 36] One of the reports described profound resistance to the vasoconstrictive effects of alpha-adrenergic agonists. The possible need for temporary cardiac pacing should be considered in patients receiving amiodarone who require general anesthesia.

Amiodarone elevates the serum digoxin level by about 50 per cent.[76] It also potentiates the anticoagulant effect of warfarin by about 100 per cent and increases the serum levels of several antidysrhythmic drugs, such as quinidine (by 33 per cent), procainamide (by 55 per cent), phenytoin, and flecainide.[70] Also, amiodarone may cause additive hemodynamic or electrophysiologic effects with drugs such as beta-blockers and calcium-channel blockers.

Dosage and Pharmacokinetics. Amiodarone is unique in that it has an extremely long half-life, variably reported from 14 to 107 days.[5] Therapeutic and steady-state plasma concentrations are achieved slowly with maintenance oral administration at 9.5 and 30 days, respectively. Upon discontinuation of the drug, therapeutic and toxic effects may persist for prolonged periods. Oral absorption of amiodarone is slow and incomplete, and bioavailability is variable and low, ranging from 22 to 50 per cent. The drug is extensively metabolized in the liver, with minimal excretion via the kidneys. Amiodarone and a major metabolite, desethylamiodarone, have a large volume of distribution and accumulate widely throughout the body. Therapeutic plasma levels range from about 0.5 to 2.5 μg per ml. Amiodarone is extensively protein-bound, primarily to albumin.

The intravenous form is not approved for use in the United States but has been administered in Europe in doses of 300 to 600 mg over a period of 20 min to 2 hours. Oral amiodarone is generally begun at about 1.2 to 1.6 g per day in divided doses for about 10 days, then decreased to 400 to 800 mg per day for about 10 days, and then decreased to 200 to 400 mg per day in one or two divided doses. The dose should be titrated downward to the minimal effective dose to suppress life-threatening arrhythmias in an attempt to avoid the serious side effects of the drug.

CLASS IV DRUGS

The main effect of class IV agents is to block the slow, inward calcium current across the myocardial cell membrane and vascular smooth muscle. Specificity for cardiac or vascular smooth muscle varies within the group, verapamil and diltiazem being more potent in cardiac tissue and nifedipine exerting most of its effect on smooth muscle.

Verapamil

Electrophysiologic Effects. Electrophysiologic effects of verapamil are seen predominantly in tissues in which phase 0 or phase 4 depolarization is calcium-dependent, namely in the SA and AV nodes. Verapamil decreases the slope of spontaneous phase 4 depolarization in SA node cells and reduces Vmax, the action potential amplitude and the maximal diastolic potential in cells of the SA and AV nodes. This class IV drug prolongs conduction time and increases the ERP of the AV node in a selective fashion. The AH interval is prolonged, and this effect is only partially reversible with atropine.[93] Verapamil prolongs the anterograde ERP of the AV node but has no effect on retrograde AV-nodal conduction time. Also, the drug does not change anterograde or retrograde conduction and refractoriness in accessory conduction pathways. In normal, fast-response cells (atrial and ventricular muscle, His Purkinje system) at therapeutic levels, verapamil has no effect on action potential amplitude, Vmax, or resting membrane potential.

However, verapamil can abolish ventricular re-entry rhythms caused by slow responses in diseased ventricles with reduced levels of membrane potential. In vitro, verapamil significantly depresses SA node rate, but in the intact individual, spontaneous heart rate decreases only minimally or not at all because of reflex sympathetic stimulation. The blocking effects of verapamil are more readily seen at faster rates of stimulation (use-dependency). Verapamil does not block beta-adrenergic receptors but does have some alpha-adrenergic blocking properties.

Electrocardiogram. The QRS and QT-c intervals are not significantly affected. The PR interval is prolonged and heart rate may be slowed.

Hemodynamics. Verapamil has significant negative inotropic properties. It also causes vasodilation in peripheral vascular beds and the coronary circulation. The vasodilating action and reflex sympathetic stimulation help to maintain cardiac output, even in the face of verapamil's myocardial depressant effects. However, cardiac output is reduced with high doses or in susceptible patients with poor ventricular function. Also, the combination of verapamil and beta-blocking agents can markedly decrease cardiac output and can cause profound hypotension.

Clinical Application. Verapamil is particularly useful in treating supraventricular tachycardias and atrial fibrillation or flutter. Intravenous verapamil is generally considered the drug of choice for terminating paroxysmal supraventricular tachycardias, which incorporate the AV node as part of the re-entrant circuit. The success rate in terminating this arrhythmia is about 80 per cent.[89] This effect is mediated by prolonging AV-nodal conduction and refractoriness and thus blocking impulse transmission through the AV node. Verapamil is also useful in slowing the ventricular response rate in atrial fibrillation and flutter. In the case of atrial fibrillation, verapamil may (1) decrease the frequency of random impulse conduction through the AV node, (2) "regularize" AV conduction at a slower rate, or (3) convert to sinus rhythm (least common occurrence).

A significant precaution in the use of verapamil to treat paroxysmal supraventricular tachycardia involves pre-excitation of the AV node in Wolff-Parkinson-White syndrome. If the supraventricular tachycardia is orthodromic (anterograde conduction through the AV node and retrograde over the accessory pathway), then verapamil has a high success rate by blocking anterograde AV nodal conduction. If the paroxysmal supraventricular tachycardia is antidromic (anterograde conduction through accessory pathway and retrograde over the AV node), successful blockade with verapamil is unlikely because it has little effect on refractoriness or conduction in accessory pathways. Atrial flutter and fibrillation also may occur in Wolff-Parkinson-White syndrome. Verapamil in this setting may be dangerous because it may shorten the ERP of the accessory pathway (via reflex sympathetic stimulation) and simultaneously block anterograde conduction in the AV node. Consequently, during atrial fibrillation or flutter in patients with Wolff-Parkinson-White syndrome, the ventricular response may be increased, which could precipitate ventricular fibrillation.[41]

Generally, verapamil is ineffective against ventricular arrhythmias. On occasion, however, verapamil may be useful in patients with arrhythmias occurring secondary to myocardial ischemia. Its effectiveness in this setting results from lowering myocardial oxygen consumption and coronary vascular resistance. In addition, verapamil may be effective in treating refractory ventricular fibrillation following cardiopulmonary bypass in patients with ventricular hypertrophy.[34]

Oral verapamil is used to prevent recurrences of supraventricular tachycardia involving AV-nodal re-entry. Concomitant administration of digitalis may enhance its effectiveness.

Side Effects and Drug Interactions. Severe hypotension, bradycardia, and asystole have been reported following intravenous use, especially with concurrent beta-blockers or in patients with sick sinus syndrome.[9, 81] Contraindications to its use include advanced heart failure, AV conduction block, sinus node disease, and significant hypotension. Constipation, nausea and vomiting, lightheadedness, orthostatic hypotension, headache, nervousness, and pruritis have been reported. Infrequently, abnormal liver transaminase tests have been observed and may necessitate discontinuation of therapy.

In laboratory studies, verapamil has been shown to depress twitch height response to indirect stimulation.[60] This suggests a potentially clinically relevant synergistic interaction with muscle relaxants. Cautious clinical attention to neuromuscular function is necessary to safely use verapamil in patients who are receiving or have recently received muscle relaxants.

Drugs with negative inotropic properties, such as beta-blockers, disopyramide, and inhalational anesthetics, should be used cautiously in conjunction with verapamil. Because the cardiovascular depressant effects of the inhalational anesthetics involve inhibition of calcium-related intracellular processes, the interaction of verapamil and these anesthetics is synergistic.[48] Concomitant administration of verapamil and quinidine may result in severe hypotension because both drugs antagonize the effects of catecholamines on alpha-adrenergic receptors. Verapamil may decrease the clearance of digoxin by about 30 per cent, with an increase in serum concentration of 50 to 70 per cent during the first week of verapamil therapy.[54]

Dosage and Pharmacokinetics. Oral verapamil is rapidly and almost completely absorbed from the GI tract. However, its bioavailability is low (only about 20 to 35 per cent) because of extensive first-pass hepatic metabolism. The drug is 90 per cent protein-bound, and up to 70 per cent of the drug is excreted via the kidneys. The duration of action is 4 to 6 hours, with an elimination half-life of 3 to 12 hours. There is marked interpatient variability in plasma levels when verapamil is given orally. Metabolism involves N-dealkylation and O-demethylation, with nor-verapamil (⅛ of the calcium-channel blocking potency of verapamil) as the major metabolite. The dose must be decreased in patients with hepatic dysfunction.

Verapamil dosage for acute intravenous treatment of paroxysmal supraventricular tachycardia is 0.07 to 0.15 mg per kg over 1 to 2 minutes, with the same dose repeated in 30 minutes if necessary. Peak hemodynamic effect is seen in 3 to 5 minutes. A constant infusion at 5 μg per kg per minute can be used to maintain its therapeutic effect. The oral dose ranges from 120 to 720 mg daily divided into three or four doses.

UNCLASSIFIED DRUGS

One of the major limitations of the Vaughan Williams classification is that it fails to include cardiac glycosides, which have considerable antiarrhythmic qualities. Although the primary therapeutic use of this group of drugs is to increase the force of cardiac contraction, a very useful secondary effect is the slowing of the ventricular response rate during atrial fibrillation or flutter. The unusually narrow

Table 3. *Effects of Digitalis on Electrical Properties of the Heart*

PROPERTY	DIRECT THERAPEUTIC EFFECT	DIRECT TOXIC EFFECT	INDIRECT EFFECT
SA-node automaticity	0*	Decrease	Decrease
Atrial conduction time	0	Increase	Decrease
Atrial refractoriness	Increase (small)	Increase	Decrease
AV node			
Conduction time	Increase (small)	Increase	Increase
Refractoriness	Increase (small)	Increase	Increase
Purkinje fiber			
Automaticity	0 or increase (small)	Increase	0
Conduction time	Increase (small)	Increase	0
Refractoriness	Increase (small)	Decrease	0
Ventricle			
Conduction time	0	Increase	0
Refractoriness	Increase (small)	Decrease	0
After-depolarizations, triggered activity	0	Increase	0

* 0 indicates negligible effect.

From Atlee JL III: Perioperative Cardiac Dysrhythmias: Mechanisms, Recognition, Management. Chicago, Year Book Medical, 1985; with permission.

therapeutic-toxic dose ratio of this group of drugs necessitates a clear understanding of their properties.

Digitalis

Electrophysiologic Effects. As with the positive inotropic effect, the antiarrhythmic effect of digitalis is a complex combination of direct and indirect actions. The primary direct pharmacologic effect of digitalis is inhibition of membrane-bound Na^+-K^+-dependent ATPase. This enzyme provides the chemical energy necessary for the transport of sodium (out) and potassium (in) during repolarization. Digitalis binds to the enzyme in a specific, saturable way that inhibits enzyme activity and impairs the active transport of sodium and potassium. The net result is a slight increase in intracellular sodium and a corresponding decrease in intracellular potassium concentration. This also results in a small net increase in calcium inside the cell in exchange for sodium.

Cells in different parts of the heart have differing sensitivities to digitalis that also vary with the concentration of the drug (Table 3). With therapeutic concentrations in the atrium, digitalis has no direct effect on sinus rate, intra-atrial conduction time, or atrial refractory period. The dominant effects are indirect and mediated by the autonomic nervous system. Toxic levels result in partial depolarization of the cells of the SA node and in suppression of normal automaticity. Therapeutic levels of digitalis in atrial muscle fibers increase maximal diastolic potential and action potential amplitude and decrease APD.

More prolonged exposure produces an opposite effect and also results in delayed after-depolarizations and repetitive firing.[47]

The direct effect of digitalis on Purkinje fibers causes an initial small increase in APD and later a decrease in APD. The slope of phase 4 depolarization is increased and the resting potential is decreased, so that the initiation of depolarization (phase 0) begins at a less negative potential; therfore, both Vmax and conduction velocity are decreased and ERP is increased. The conduction velocity can become so depressed that ultimately the fibers become unexcitable. The effect of digitalis on spontaneous phase 4 depolarization depends on the extracellular potassium concentration. At low concentrations of potassium, the increased rate of phase 4 depolarization is augmented and automaticity increases. At higher potassium concentrations (>4 mEq per L), delayed after-potentials may appear, which may be sufficient to reach threshold and trigger depolarization. Thus, digitalis can cause ectopic impulses by two separate mechanisms: (1) enhanced normal automaticity, and (2) development of delayed after-depolarizations and triggering.

The direct effects of digitalis on ventricular muscle fibers are similar to those on Purkinje fibers. High concentrations decrease conduction velocity and eventually cause inexcitability. Digitalis does not enhance spontaneous phase 4 depolarization in ventricular muscle fibers but may produce delayed after-depolarizations.

In the AV node, the indirect effects of digitalis are most prominent, but at high concentrations, the drug will cause direct depression of AV nodal conduction and increase refractoriness. Ultimately, AV block is produced.

The indirect effects of digitalis are complex and not completely understood. It is thought that digitalis enhances efferent vagal activity and causes a reflex-induced decrease in sympathetic tone. However, toxic levels can augment sympathetic activity and result in ventricular tachyarrhythmias.

The AV node is the portion of the conduction system most strongly influenced by both direct and indirect effects of digitalis. Conduction through the AV node is slowed, and the ERP of the AV node is lengthened.

In atrial tissue, the direct and indirect (vagal) effects of digitalis are opposed. The direct effect is an increase in APD, but the indirect effects (mediated by acetylcholine release) are marked decreases in APD and ERP. At therapeutic concentrations, the indirect effect predominates, which makes the atria responsive to higher stimulation frequencies. Therefore, the effectiveness of digitalis in reducing the ventricular response rate in cases of atrial fibrillation and atrial flutter is, in part, a paradox. The frequency of atrial impulses arriving at the AV node generally increases, which leads to frequent partial depolarization (called concealed conduction). This effect is mitigated by the increased AV nodal ERP (due to direct effects, vagal effects, and sympatholytic effects) and results in a net decrease in the frequency

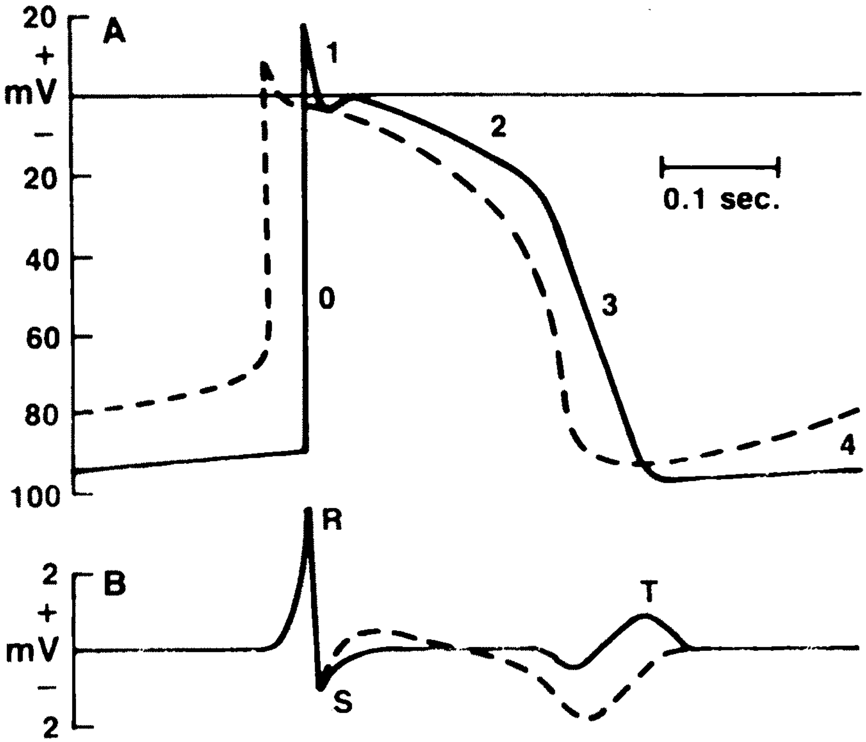

Figure 1. Schematic representation of the effects of digitalis (*dashed line*) on the Purkinje fiber potential (*A*) and a unipolar electrocardiogram recorded from the same preparation (*B*). (*A*) after the effects of digitalis have developed, there is a decrease in the maximum diastolic potential, an increase in the slope of spontaneous phase 4 depolarization (normal automaticity), and a decrease in action potential duration. Because of the increase in the slope of phase 4 depolarization, the fiber becomes automatic. The level of transmembrane potential at which activation occurs (threshold potential, phase 0) shifts to a more positive value, and the amplitude of the action potential decreases. (*B*) Because of the changes in the slope and duration of phases 2 and 3 of the action potential (*A*), there is a change in the ST segment and T wave of the unipolar electrogram and a decrease in the RT interval. (*From* Atlee JL III: Perioperative Cardiac Dysrhythmias: Mechanisms, Recognition, Management. Chicago, Year Book Medical, 1985, p 317; with permission.)

of impulses that successfully traverse the AV node to depolarize the His Purkinje system.

Electrocardiogram. Digitalis may slow the sinus rate and certainly will blunt the response to exercise. The QT interval may be decreased because of decreased APD. The PR interval lengthens. Characteristic ST-segment and T-wave changes occur because of effects of digitalis on phases 2 and 3 of the action potential (Fig. 1). Generally, the T-wave amplitude is reduced, and the ST segment is depressed and shortened, with the occasional appearance of a prominent U wave.

Hemodynamics. The overall effects of digitalis on hemodynamics result from the interplay of its positive inotropic effect, change in heart rate, and effects on the autonomic nervous system and vascular smooth muscle. Also, the effect of digitalis on the circulatory system varies depending on the baseline cardiac function of the individual. In normal hearts, digitalis increases contractility but also decreases heart rate and increases systemic vascular resistance and venous tone, so that cardiac output remains constant or may decrease slightly.[97] In patients with heart failure, the direct positive inotropic action of digitalis predominates, which results in increased stroke volume, decreased heart size, and more efficient contraction. Because of the improved circulation, sympathetic activity and venous tone are reflexly decreased; this decreases left ventricular afterload and further improves cardiac function. This general improvement in cardiac function and decreased sympathetic outflow improves renal perfusion and clearance of salt and water. Digitalis also decreases heart rate, either by a reduction in sinus rate or in the ventricular response during atrial flutter or fibrillation.

Clinical Application. Digitalis is used primarily to treat heart failure but can be valuable in managing certain types of supraventricular tachycardias. Digitalis is used most commonly to slow the ventricular response during atrial flutter or fibrillation and may also be useful in treating paroxysmal supraventricular tachycardias (if it is not caused by digitalis). It should not be used to treat atrial flutter or fibrillation in patients with Wolff-Parkinson-White syndrome because the drug may shorten refractoriness in the accessory pathway and speed the ventricular response.

Side Effects and Drug Interactions. Toxic reactions to digitalis are frequent and may be lethal. Gastrointestinal and neurologic side effects may be early signs of digitalis intoxication. Nausea, vomiting, abdominal pain, anorexia, and diarrhea may occur; fatigue, depression, visual changes, personality disorders, drowsiness, and headache are reported. In some patients, disturbances of cardiac rhythm may be the first sign of digitalis intoxication. Almost any rhythm disturbance or conduction abnormality may occur, but the most common are multi-form, premature ventricular beats, atrial tachycardia with block, and nonparoxysmal AV junctional tachycardia. Digitalis may cause marked sinus bradycardia, high levels of AV block, ventricular tachycardia, and ventricular fibrillation. Cardiac toxicity is most likely to occur in patients with severe underlying heart disease. Many factors increase the toxicity of digitalis, such as catecholamines, hypokalemia, hypercalcemia, hypomagnesemia, hypoxia, and acid-base imbalance.

Nonabsorbable antacids, kaolin-pectin, cholestyramine, and neomycin may decrease absorption of digoxin when it is administered orally. A significant drug interaction occurs when quinidine is added to a maintenance digoxin regimen.[13] Because it decreases both the renal and nonrenal elimination of digoxin and also appears to decrease its apparent volume of distribution, quinidine increases the serum level of digoxin. The average increase is twofold, although there is wide variability among patients. In addition to quinidine, concentrations of digoxin in plasma are also increased by quinine, verapamil, and amiodarone. Diuretics enhance the likelihood of digitalis toxicity by producing electrolyte imbalance and decreasing glomerular filtration rate. Whether digitalis toxicity is enhanced by anesthetics is controversial. The use of electrical countershock to treat digitalis-toxic arrhythmias is hazardous because severe conduction abnormalities and ventricular arrhythmias may result.

Dosage and Pharmacokinetics. Because digoxin is most commonly used, this section will focus primarily on that drug. Wide variability in bioavailability is a significant clinical problem with tablets from different manufacturers. The half-life is about 1 to 2 days with peak effects seen about 2 to 3 hours after oral administration. Intravenous digoxin reaches peak effects in 1.5 to 2 hours but has a significant effect within 5 to 30 minutes. Digoxin is approximately 25 per cent protein-bound, and the therapeutic range of plasma concentrations is 0.5 to 2.0 ng per ml. For a given serum level, myocardial accumulation is greater in infants and children.[7] Digoxin has a high apparent volume of distribution (6 L per kg), which is decreased in elderly patients and those with impaired renal function. Approximately 50 to 75 per cent of digoxin is excreted unchanged in the urine.

The average intravenous digitalizing dose in adults is 0.5 to 1.0 mg, with 0.25 to 0.5 mg given initially and 0.25 mg at 4- to 6-hour intervals. The daily maintenance intravenous dose is 0.125 to 0.5 mg, which may be given in incremental doses. The average oral digitalizing dose is 0.75 to 1.5 mg, with a daily maintenance dose of 0.125 to 0.5 mg. In children, appropriate digoxin doses are controversial and vary considerably depending on the age of the patient.

The usual initial intravenous dose of ouabain is 0.25 to 0.5 mg in adults, with the onset of activity occurring within 3 to 10 minutes and the peak effect at 30 minutes. Subsequent to the initial dose, 0.1-mg increments can be given at 30-minute intervals; the total dose within the first 24 hours should not exceed 1.2 mg.

Adenosine

Adenosine, a naturally occurring compound found in every cell of the human body, has been used as an antiarrhythmic agent in Europe since 1955,[46, 58] but its use in the United States is still investigational. Adenosine is reviewed here briefly because it may prove valuable, particularly for arrhythmias occurring during anesthesia.

Electrophysiologic Effects. Adenosine causes SA node depression, slows AV conduction, and decreases atrial contractility.[28, 29] This drug has indirect effects that can be observed only when cyclic AMP (cAMP) has been elevated, as, for example, by beta-adrenergic agonists. Adenosine in this setting exerts a negative inotropic effect to attenuate the positive inotropic action of these substances and reduce cAMP levels. Adenosine also depresses ventricular automaticity and attenuates the release of norepinephrine induced by adrenergic nerve stimulation via a presynaptic action.[67] Adenosine can decrease calcium influx into cells, can diminish the amplitude of depolarizing after-potentials, and can terminate triggered activity. Adenosine hyperpolarizes atrial myocardial cells and decreases their APD via an increase in outward K^+ current.

Electrocardiogram. Adenosine can cause sinus bradycardia and sinus arrest. It can also cause pacemaker shift. Adenosine increases AH interval and may result in complete AV block.

Hemodynamics. Adenosine is a potent systemic and coronary vasodilator. However, generally there is no marked reflex tachycardia or increases in myocardial contractility, catecholamines, or renin-angiotensin. Cardiac output is well maintained and tachyphylaxis does not occur.

Clinical Application. Adenosine is frequently used in Europe for induced hypotension with a marked advantage of ease of titration because of its short half-life.[16, 104] Adenosine is highly effective in terminating paroxysmal supraventricular tachycardias involving the AV node.[111] This drug has also been used as a diagnostic tool for tachyarrhythmias that do not involve the AV node in their re-entrant circuit (for example, unmasking atrial flutter by blocking AV nodal conduction). Adenosine has been used in the diagnosis of sick sinus syndrome after prophylactic insertion of a temporary pacemaker[10] and is extremely effective in terminating catecholamine-mediated ventricular tachycardia.[63] A possible role for adenosine has been suggested in the therapy of ventricular arrhythmias seen with the halothane-epinephrine interaction.[72]

Side Effects and Drug Interactions. The use of adenosine in awake patients is difficult because of symptomatic dyspnea and a feeling of suffocation. The drug also causes flushing and may provoke bronchospasm in patients with asthma. Headache, back pain, abdominal pain, chest cramps, blocked nose, and dry mouth have been reported.[24] Profound bradycardia, heart block, new onset of atrial fibrillation, and cardiac arrest have also been known to occur.[112]

Dipyridamole, a known inhibitor of adenosine uptake, potentiates the effect of the drug. Cardiac glycosides, verapamil, and benzodiazepines have also been reported to potentiate adenosine in the experimental setting. Aminophylline and other methylxanthines antagonize the effects of adenosine.[8]

Some authors[32] have suggested that adenosine may be contraindicated in patients with coronary occlusive disease because of the potential for "coronary steal" induced by its profound vasodilation. At present, conclusions cannot be drawn and further study is indicated.

Dosage and Pharmacokinetics. Adenosine's actions are rapidly terminated by tissue wash-out or by cellular uptake and metabolism. The drug can be degraded to either adenosine monophosphate or inosine, which is further metabolized to hypoxanthine. The half-life of adenosine is less than 10 seconds.[53]

Optimal doses of adenosine depend on the mode of administration and individual variability. Increasing bolus doses of adenosine beginning with 40 μg per kg have been used to a possible maximal dose of 200 μg per kg[111]; the mean effective dose was 8.8 ± 2.6 mg of adenosine alone, which was reduced to 1.0 ± 0.52 mg when dipyridamole was used for pretreatment.

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Electrical Treatment of Arrhythmias

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Atrial or ventricular pacing, cardioversion and defibrillation frequently offer very rapid, easily controlled, definitive therapy for a wide variety of intraoperative arrhythmias. This article stresses the mechanism of action of electrical therapy and puts into perspective the relationship of this therapeutic modality with drug therapy and vagal maneuvers.

PATHOPHYSIOLOGY

Re-entry

During re-entry, an impulse activates one area of myocardial tissue and abnormally returns to reactivate the identical area. The requirements for the existence of re-entry include a complete circuit, unidirectional block, and decreased conduction velocity in one limb of the circuit.[19] The phrase "unidirectional block" does not necessarily imply that the block must be permanent. The completely repolarized limb can conduct an impulse while the other limb remains absolutely refractory to the impulse. Transient block that occurs when two limbs of the circuit have markedly different refractory periods can be just as important in the genesis of re-entrant arrhythmias as permanent block.[3] Ischemia, one cause of transient block, depolarizes myocardial cells nonhomogeneously and slows conduction velocity. Therefore, re-entrant arrhythmias can and do occur in the presence of ischemia.

Re-entrant arrhythmias are classified according to the size and the orderliness of the pathway. Macro-re-entrant circuits can include an entire atrium, or the atrioventricular (AV) node plus sections of the atrium and ventricle. Several examples of macro-re-entry include AV nodal reciprocating tachycardia (Wolff-Parkinson-White syndrome), AV-nodal re-entrant tachycardia, and ventricular tachycardia (VT). Micro-re-entrant pathways might include only small groups of cells.

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Typical examples of micro-re-entrant arrhythmias are atrial and ventricular fibrillation.

Automaticity

Automaticity, a molecular process by which cells spontaneously depolarize during phase 4 of the action potential, normally occurs in sinoatrial (SA) and AV-nodal cells. Automaticity can also occur in cells around the coronary sinus, cells of the tricuspid and mitral valves, and the cells of the His Purkinje system.[4, 38] Enhanced automaticity occurs when the slope of phase 4 of the action potential changes in normally automatic cells. If the slope of phase 4 increases in the SA node, the cells reach threshold more quickly, and the heart rate increases. If the slope of phase 4 decreases, then the heart rate would decrease. Volatile anesthetics decrease the slope of phase 4, slowing heart rate.[21]

In contrast to SA or AV cells, muscle cells of the atrium and ventricle do not normally display automaticity. However, if the cells are partially depolarized, they can exhibit abnormal automaticity.[5, 20, 23] Ischemia partially depolarizes the muscle cell by permitting an outward leakage of potassium. Calcium-related abnormal automaticity causes arrhythmias by creating automatic or ectopic foci. If phase 4 of the abnormally automatic ectopic focus is very rapid, then that focus will control the heart rate. Parasystole occurs when the ectopic focus exhibits entry blockade. In this case, a normal sinus impulse cannot overdrive the ectopic focus.

Triggering

Triggered arrhythmias occur when low amplitude early or delayed after-depolarizations reach threshold and stimulate a train of secondary depolarizations.[7] The difference between abnormal automaticity and triggering is that triggered arrhythmias require an initiating depolarization.[7, 40] A pacemaker impulse can serve as an initiating event for triggered arrhythmias. Cardiac glycosides are associated with triggered arrhythmias.[14]

MECHANISM OF ACTION OF ELECTRICAL THERAPY

Electrical therapy, both pacing and cardioversion, terminates arrhythmias by depolarizing at least one limb of the re-entrant circuit, blocking conduction in that limb. This prevents the impulse from returning to the origin of the circuit, completing the re-entrant pathway. This electrically induced block is not permanent so the arrhythmia can recur.

Re-entrant Arrhythmias

Re-entrant arrhythmias are easily treated with single or multiple pacing stimuli or cardioversion. Macro-re-entry responds either to overdrive suppression by pacing or to cardioversion.[31] Macro-re-entry that includes the AV or SA node could also respond to vagal stimulation. Microentry usually requires defibrillation of the ventricle or cardioversion of the atrium. Fibrillation patterns do not respond to pacing techniques possibly because an overwhelming number of re-entrant circuits block the single stimulating focus located at the pacing electrode. Therefore, a micro-re-entrant arrhythmia such as ventricular fibrillation (VF) requires defibrillation, whereas AV-nodal re-entrant tachycardia, a macro-re-entrant arrhythmia that includes the AV node, should convert to sinus rhythm with vagal maneuvers, rapid atrial pacing, or cardioversion. Re-entrant atrial tachycardia, a re-entrant arrhythmia that does not include the SA or the AV node, is not affected by changes in vagal tone but does respond to rapid atrial stimulation and cardioversion.

Automatic Arrhythmias

Introducing premature stimuli will not convert an automatic arrhythmia to sinus rhythm. Rather premature depolarizations reset the rate of the automatic focus. A supraventricular tachycardia (SVT) that responds to rapid atrial pacing by rate changes rather than by termination of the arrhythmia should be thought of as an automatic arrhythmia and treated with intravenous drugs or cardioversion.

Triggered Arrhythmias

Calcium-loaded myocardial cells respond to previous impulses by abnormally depolarizing during the repolarizing period. These abnormal depolarizations are called after-depolarizations and are responsible for triggered arrhythmias. The electrocardiographic appearance of a triggered arrhythmia is essentially indistinguishable from an automatic arrhythmia. Clinically, one cannot discriminate triggering from abnormal automaticity as a cause for atrial flutter with varying block. As stated previously, triggered arrhythmias require an initiating stimulus such as the output of a pacemaker. Therefore, if an SVT does not respond to rapid atrial pacing, one must consider not only automaticity but also triggering as a potential cause of the arrhythmia.

ELECTRICAL TECHNIQUES

Pacing

Ventricular pacing is effected with endocardial electrodes inserted transvenously or through special ports on pulmonary artery catheters, via electrodes incorporated into balloon flotation catheters (both as an adjunct to a standard pulmonary artery catheter and on those designed only for pacing), with epicardial electrodes sutured or screwed into the myocardium and with recently perfected transcutaneous paddles. The last technique is not yet widely available. With that exception, ventricular pacing is a very familiar technique and will not be described in detail.

Atrial pacing is most often employed after cardiac surgery utilizing electrodes sutured directly to the atrial wall. Most commonly unipolar pacing with only one electrode is used. However, bipolar pacing offers the advantages of less interference with the electrocardiogram (ECG) (smaller pacing artifact) and better recording of atrial electrograms (see following). Atrial pacing is also possible after inserting special electrodes through pulmonary artery catheters. Atrial pacing is then achieved using standard pulse wave generators. Rapid atrial pacing, stimulating the atrium at rates of 200 to 450 in order to interrupt atrial arrhythmias, requires a special generator capable of providing such rapid rates.

USE OF ATRIAL ELECTRODES TO DIAGNOSE ARRHYTHMIAS

One of the difficulties encountered in diagnosing arrhythmias is accurate definition of atrial activity. The atrial electrogram provides a very rapid technique to determine not only the existence and frequency of atrial activity, but also the relationship of atrial to ventricular depolarizations. The bipolar atrial electrogram recorded between two atrial electrodes, demonstrates a very small R wave, making it easy to distinguish atrial and ventricular signals. The unipolar atrial electrogram is often confusing because the P and R waves are of equal amplitude. If bipolar recordings are unavailable, this problem can be obviated by simultaneous recording of both the atrial electrogram and a surface ECG. This technique, by clearly locating the R waves on the surface ECG, will aid in separation of P and R waves on the atrial electrogram (Fig. 1). Esophageal electrodes are an acceptable alternative to atrial electrodes.[22]

DIRECT CURRENT CARDIOVERSION AND DEFIBRILLATION

Mechanism

Direct current (DC) cardioverting and defibrillating impulses uniformly depolarize excitable atrial and ventricular cells without interrupting membrane integrity. In this way, both micro-re-entrant and macro-re-entrant circuits are interrupted and therefore eliminated as a cause of the arrhythmia. Several older investigations imply that myocardial function decreases because pulmonary edema developed following cardioversion.[28, 33] More recent evidence suggests that global myocardial function does not deteriorate after cardioversion.[24] A clinical study of 30 patients revealed an increase in total CPK without a

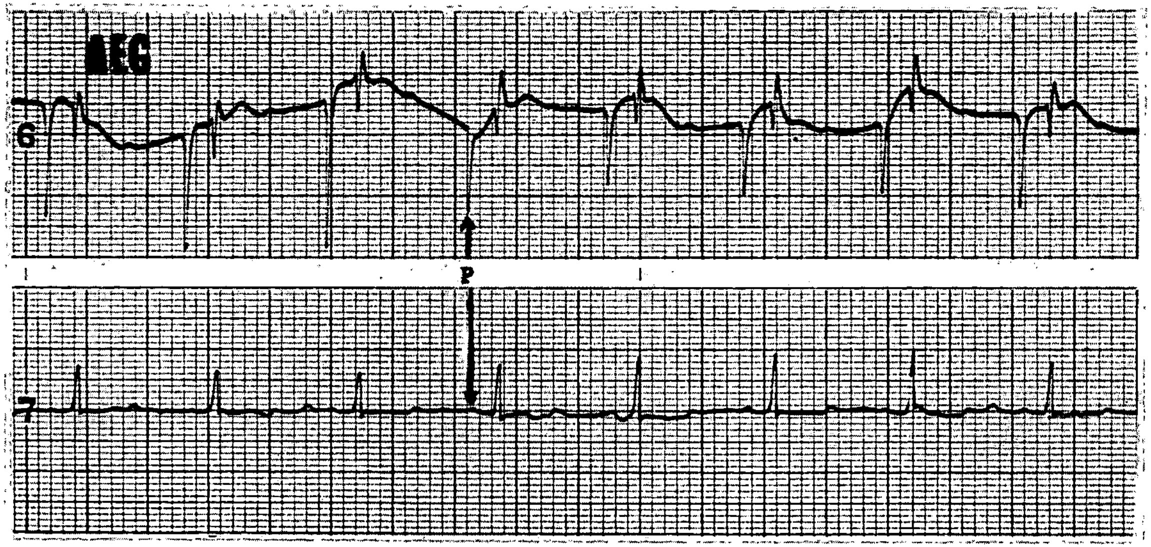

Figure 1. The atrial electrogram (*upper strip*) recorded from inside the atrium reveals large atrial depolarization waves that could be mistaken for QRS complexes if a surface lead (*lower strip*) were not simultaneously recorded.

significant increase in the MB fraction.[11] Myocardial damage from heat and electrical energy can be minimized by use of larger paddles to decrease thoracic resistance, applying the cardioverting impulse to a larger area of myocardium, waiting longer time intervals between impulses, and using fewer impulses with a higher energy level.[8, 9, 30, 34] Some controversy exists concerning the energy dose required for defibrillation. Geddes et al[18] suggested that the defibrillating success rate using 300 J decreased as the weight of the patient increased. Conversely, Adgey et al[2] using 150 to 165 J energy levels successfully defibrillated 85 per cent of the patients with one shock and 99 per cent of the patients with the third shock. Other investigators also have shown that there is no relationship between energy levels and defibrillating success related to body weight.[16, 26] In an emergency, use 200 J for the first shock and 200 to 300 J for the second. If the patient develops VF again, it is not necessary to increase the energy level of the impulse.[36]

Defibrillating the Patient with a Permanent Pacemaker

New pacemakers, including the automatic defibrillator, are protected against defibrillating impulses of up to 400 J. Since the leads can conduct the impulse to the myocardium, it is recommended that the defibrillator electrodes be placed 5 or more inches away from the implanted pacemaker in the anterioposterior position. The energy levels recommended by the American Heart Association should not damage the pacemaker.

Many factors determine the success rate of cardioverting and defibrillating impulses.[27] Of primary importance are the factors that affect transthoracic resistance. Pressing the paddles forcefully against the chest wall reduces the transthoracic resistance and increases the current to the myocardium.[25] Increasing the diameter of the paddles decreases resistance to a limit; however, very large paddles apparently spread the current over too wide an area to defibrillate the myocardium.[6, 12, 37] Applying the impulse during expiration increases the success rate of defibrillation.[13]

Indications

Cardioversion is indicated as first-line therapy whenever acute onset of an arrhythmia creates hemodynamic instability. Patients most susceptible to this are those requiring synchronized atrial contraction to maintain ventricular filling (for example, mitral or aortic stenosis, decreased left ventricular compliance secondary to ischemic heart disease). Cardioversion should not be used to treat the arrhythmias associated with cardiac glycoside toxicity because of the possibility of developing ventricular arrhythmias and complete heart block. Cardioversion has a low success rate in patients who experience arrhythmias secondary to enhanced or abnormal automaticity.

Defibrillation is obviously required in the presence of ventricular fibrillation.

ELECTRICAL TECHNIQUES FOR CONTROL OF ARRHYTHMIAS

This section discusses each arrhythmia and places into perspective the relationship of drug therapy, pacing, cardioversion, and vagal stimulation.

Sinus Bradycardia

Sinus bradycardia does not require treatment if it is not associated with other hemodynamic changes in an otherwise healthy individual. The first line of therapy is to eliminate the underlying cause. Hypoxia, drugs such as anticholinesterases, deep anesthesia, and reflexes related to peritoneal traction or hypertension can initiate sinus bradycardia. When specific drug therapy is required, atropine is a reasonable choice providing that hypertension is not the primary cause. After cardiac surgical procedures, however, pacing can obviate the sometimes unpredictable response to atropine. Atrial pacing should be used at a physiologic rate to maintain appropriate blood pressure and cardiac output (Fig. 2). Ventricular pacing will not preserve the atrial contribution to cardiac output and should not be used when the patient experiences sinus bradycardia.

Sinus Tachycardia

The increase in rate represents a response to an underlying physiologic disturbance. Common etiologies include hypoxemia, hypercarbia, hypovolemia, and light anesthesia, and initial therapy is directed toward alleviating these causes. Beta blockade remains the mainstay of drug therapy for sinus tachycardia. Pacing does not play a role except for very rare and unusual situations when correcting the underlying cause and appropriate drug therapy does not slow the rate, and it is imperative to do so. Atrial pacing at rates fast enough to create AV blockade can be used to slow the ventricular rate. This technique is an extreme measure that should seldom, if ever, be necessary.

Sinoatrial Nodal Re-entrant Tachycardia

One type of re-entrant SVT appears exactly like sinus tachycardia on the surface ECG. Re-entry involving the sinus node rarely occurs. It is difficult to distinguish from sinus tachycardia, except that the re-entrant tachycardia suddenly develops during one cardiac cycle, whereas sinus tachycardia is gradual in onset. SA-nodal re-entry responds to vagal stimulation, burst pacing, or administration of calcium-channel blocking agents and erroneously leaves the impression that "sinus tachycardia" can be remedied with such maneuvers. Although it is true that vagal maneuvers will slow sinus tachycardia, the rate usually increases again when vagal stimulation ceases. The tachycardia associated with SA-nodal re-entry stops suddenly with vagal stimulation or atrial pacing and the heart rate does not increase again.

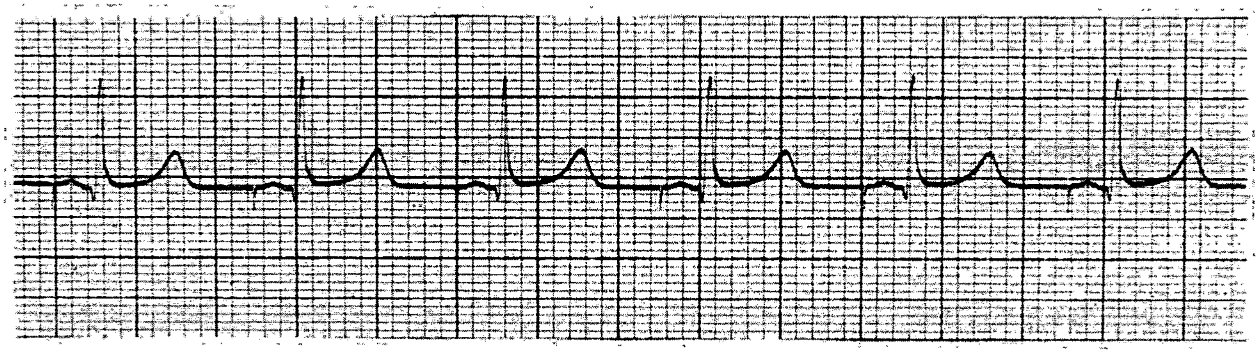

Figure 2. Standard atrial pacing must have P waves immediately following each atrial pacing impulse and a normally configured QRS complex. (*From* Zaidan JR: Electrocardiography. *In* Barash PG, Cullen BF, Stoelting RK (eds): Clinical Anesthesia. Philadelphia, Lippincott, 1989, p 616; with permission.)

Atrial Flutter

Atrial flutter is characterized by inverted P waves or flutter waves along the baseline, and is frequently associated with 2:1 AV block and a ventricular rate of 150 (Fig. 3). Electrophysiologically, automaticity or re-entry could cause atrial flutter. Re-entry is the generally accepted pathophysiologic mechanism, although it is not clear if the arrhythmia is secondary to micro-re-entry or macro-re-entry. One may consider using either drug therapy, cardioversion, or pacing to terminate atrial flutter. Control of ventricular rate is the prime goal of intraoperative therapy. In the stable patient, pharmacologic control of rate is appropriate and fortunately, will commonly convert the rhythm to sinus. Hemodynamically unstable patients require immediate synchronized cardioversion. Starting with an energy level of 25 J, increase the level to 50, 100, and finally 200 J, although high levels are usually unnecessary because this rhythm is very responsive to cardioversion.

Pacing has advantages over drug treatment and cardioversion because pacing will rapidly and painlessly terminate type I atrial flutter (atrial rate of 240 to 340). When the atrial rate is greater than 340 (type II flutter) pacing is usually ineffective. Several pacing techniques are useful in terminating the arrhythmia. Underdrive pacing uses a routine external asynchronous pacemaker set at a physiologic rate to fortuitously interrupt the re-entrant circuit and stop the arrhythmia.[1, 15, 29] Although this method is simple, regrettably it is often ineffective in terminating re-entrant arrhythmias. The second pacing method is to introduce programmed premature stimuli.[31] This very successful method requires a special pacemaker that paces the atrium and delivers one or two premature extrastimuli at predetermined intervals. These intervals must be determined through electrophysiologic testing.[35] The final method of terminating atrial flutter is burst suppression (rapid atrial pacing) and requires an external pacemaker that can produce impulses at rates up to 800 per minute. In this method, the patient is atrially paced for several seconds, approximately 10 beats per minute above the intrinsic atrial rate. The pacemaker may then be gradually or abruptly stopped. If the arrhythmia continues, repeat the same technique, increasing the pacing rate 25 per cent above the intrinsic rate. Pacing higher than 35 per cent above the intrinsic rate could convert the rhythm to atrial fibrillation. It is often advisable to institute pharmacologic therapy after cardioversion to prevent reoccurrence of flutter.

Atrial Fibrillation

The acute onset of atrial fibrillation in patients with mitral stenosis, aortic stenosis, or high left ventricular filling pressures can be associated with significant decreases in blood pressure and cardiac output. If urgent therapy is necessary, cardioversion is the treatment of choice; otherwise drugs can be administered to slow and control the ventricular response.

Pacing techniques have no role in converting atrial fibrillation to

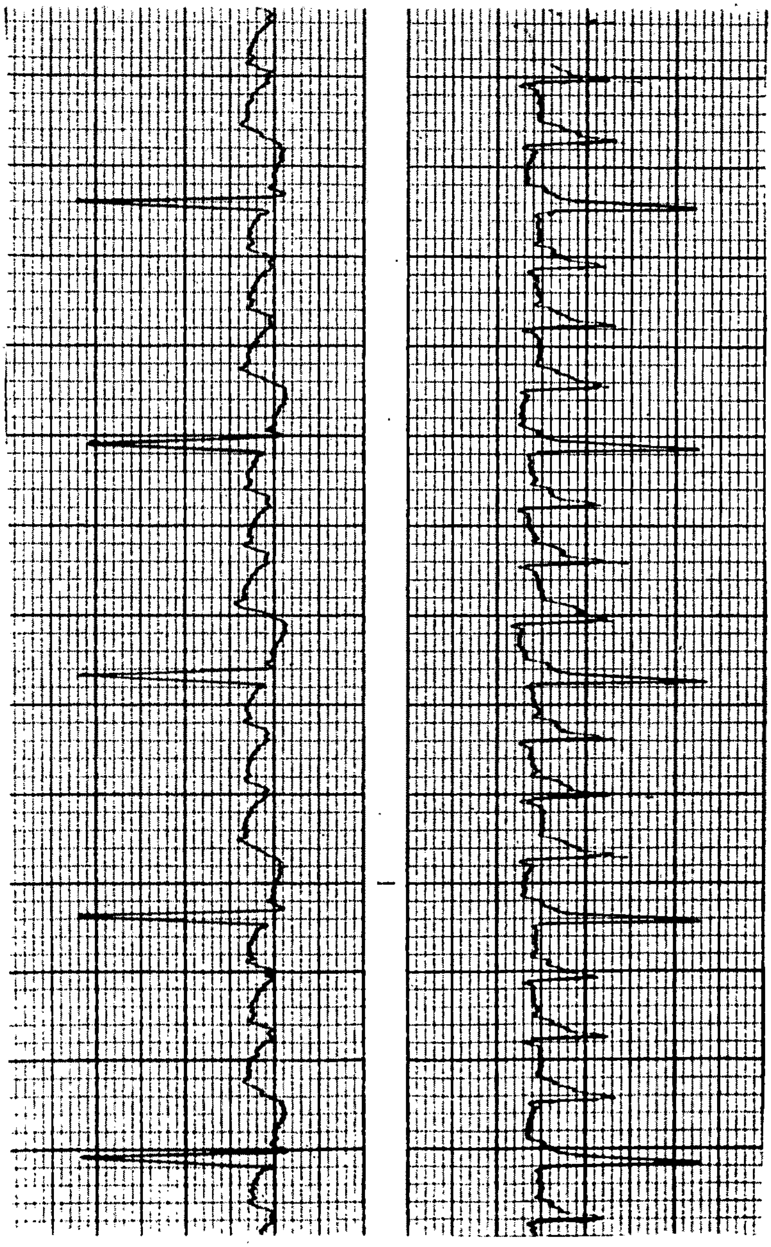

Figure 3. The top tracing is the surface ECG demonstrating characteristic saw-tooth flutterwaves. The atrial electrogram (*bottom trace*) clearly shows the regular atrial activity of atrial flutter. (*From* Zaidan JR: Electrocardiography. *In* Barash PG, Cullen BF, Stoelting RK (eds): Clinical Anesthesia. Philadelphia, Lippincott, 1989, p 601; with permission.)

sinus rhythm. However, consider using ventricular pacing to increase the heart rate in patients in chronic atrial fibrillation who are bradycardic. Some patients require a permanent ventricular-inhibited pacemaker for this reason. When using ventricular pacing, adjust the current output to the lowest possible setting and the R-wave sensitivity to approximately 3 to 5 mV. Slowly increase the current output until electrical capture occurs (Fig. 4). Add 2 to 3 mA to this threshold level for a safety factor. Adjusting the R-wave sensitivity to 3 to 5 mV will allow sensing of the R wave without sensing of the T wave or myopotentials associated with shivering.

Atrioventricular Nodal Re-entrant Tachycardia

Re-entry can occur entirely within the AV node. Therapy should terminate the tachycardia and prevent recurrent attacks. Like many other arrhythmias encountered in the intraoperative setting, the urgency and choice of treatment depends on the patient's cardiovascular function. If the patient is on the verge of hemodynamic collapse, then R wave-synchronized, emergency cardioversion is the only choice. Under less emergent conditions, vagal stimulation, drugs, or pacing are effective options. A variety of pacing techniques may be utilized. Programmed stimulation and burst stimulation work well but often are unavailable whereas underdrive pacing is least effective.

AV pacing with an AV interval of 50 msec can also be used. Contrast the AV interval of 50 msec with the typical interval of 175 to 225 msec used during routine AV sequential pacing (Fig. 5).

Atrioventricular Reciprocating Tachycardia

Patients with AV-nodal bypass tracts, such as the Bundle of Kent, experience re-entrant arrhythmias whose pathway includes atrial and ventricular muscle, the Bundle of Kent, and the AV node. The ECG is characterized by a shortened PR interval and a delta wave. Clinically, the patients require therapy when they experience repeated bouts of re-entrant tachycardia associated with clinical symptoms such as angina, shortness of breath, or dizziness. Hemodynamically unstable patients must be immediately cardioverted. If atrial pacing electrodes are available, then burst pacing is a reasonable alternative to cardioversion. Underdrive atrial or ventricular pacing is useful because an appropriately timed impulse should terminate the tachycardia. Either atrial or ventricular pacing can be used because the re-entrant circuit includes both chambers. Other applicable pacing techniques include AV sequential pacing or simultaneous AV stimulation. Atrial fibrillation associated with an extremely rapid ventricular response could occur after atrial pacing in patients with a very short refractory period of the accessory pathway.

Atrial Tachycardia

Atrial tachycardias can have several electrophysiologic mechanisms. Ectopic atrial tachycardia and multifocal atrial tachycardia are automatic arrhythmias associated with myocardial infarction, electro-

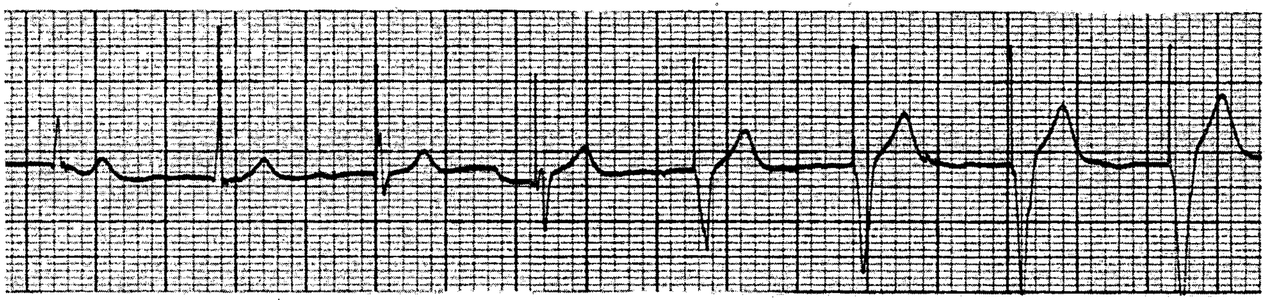

Figure 4. Normal ventricular inhibited pacing at a rate close to the intrinsic rate reveals, in sequence, a junctional escape beat, two pseudofusion beats (the ventricular pacing spike without capture deforms the junctional complex), three fusion beats (combination of junctional and paced beat), and two ventricular paced beats. (*From* Zaidan JR: Electrocardiography. *In* Barash PG, Cullen BF, Stoelting RK (eds): Clinical Anesthesia. Philadelphia, Lippincott, 1989, p 617; with permission.)

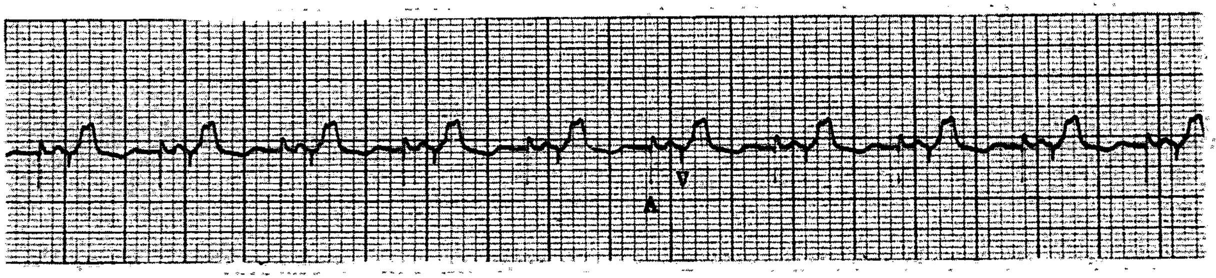

Figure 5. Sequential pacing has two impulses, each of which must be followed by a depolarization wave (P wave or QRS). The AV interval can be varied to achieve maximal cardiac output at any given pacing rate.

lyte disturbance, and severe chronic lung disease. Because they are automatic in nature, ectopic and multifocal atrial tachycardia will not respond to pacing techniques. Vagal stimulation could slow the rate for a short period of time, but it will not terminate the arrhythmia. Drug administration and cardioversion are the only means of therapy.

Electrocardiographically, intra-atrial re-entrant tachycardia is indistinguishable from automatic atrial tachycardia. Although pacing techniques could be successful, vagal maneuvers will not terminate the arrhythmia, because neither the AV nor SA nodes are included in the re-entrant circuit.

Junctional Rhythms

Occasionally, cells in the AV node or Purkinje fibers in the bundle of His take control of the heart rate. The result is loss of atrial kick and decreased blood pressure. Because the atria and ventricles simultaneously contract, cannon waves become evident on the central venous pressure tracing. In certain instances, pacing techniques are helpful (Fig. 6). Atrial pacing at a rate slightly higher than the intrinsic rate will restore the atrial kick and increase blood pressure if AV conduction remains intact in the presence of a junctional rhythm with a rate less than 70. Junctional tachycardia (rate 70 to 100) and accelerated junctional tachycardia (rate > 100) requires faster pacing rates. It might be necessary to administer a beta-blocking agent to slow the junctional rate and then to begin atrial pacing. In the presence of AV block, the AV sequential pacing is required.

Ventricular Escape Beats

Slow sinus rates are sometimes associated with occasional ventricular contractions. Atropine administration should increase the sinus rate and eliminate the ventricular escape beats. Atrial pacing at a physiologic rate avoids drug-induced tachycardia and also eliminates the arrhythmia. Parasystolic ventricular escape beats do not respond to pacing because the electrical impulse cannot enter the parasystolic area. In this case, standard drug therapy terminates the ventricular arrhythmia while atrial pacing maintains a physiologic heart rate. Do not overdrive pace patients experiencing sinus tachycardia associated with ventricular escape beats. These patients should receive standard drug therapy aimed at slowing the heart rate.

Ventricular Tachycardia

Cardioversion remains the best therapy to terminate VT. Patients experiencing VT associated with a re-entrant mechanism also respond to rapid ventricular pacing techniques similar to the methods used to terminate SVT (Fig. 7). In this instance, increase the pacemaker rate for several seconds to 10 per cent greater than the intrinsic ventricular rate; then decrease the pacemaker rate to a physiologic rate. Ventricular tachycardia greater than 180 beats per minute requires a special rapid pacing generator. Use a rate 25 per cent greater than the intrinsic

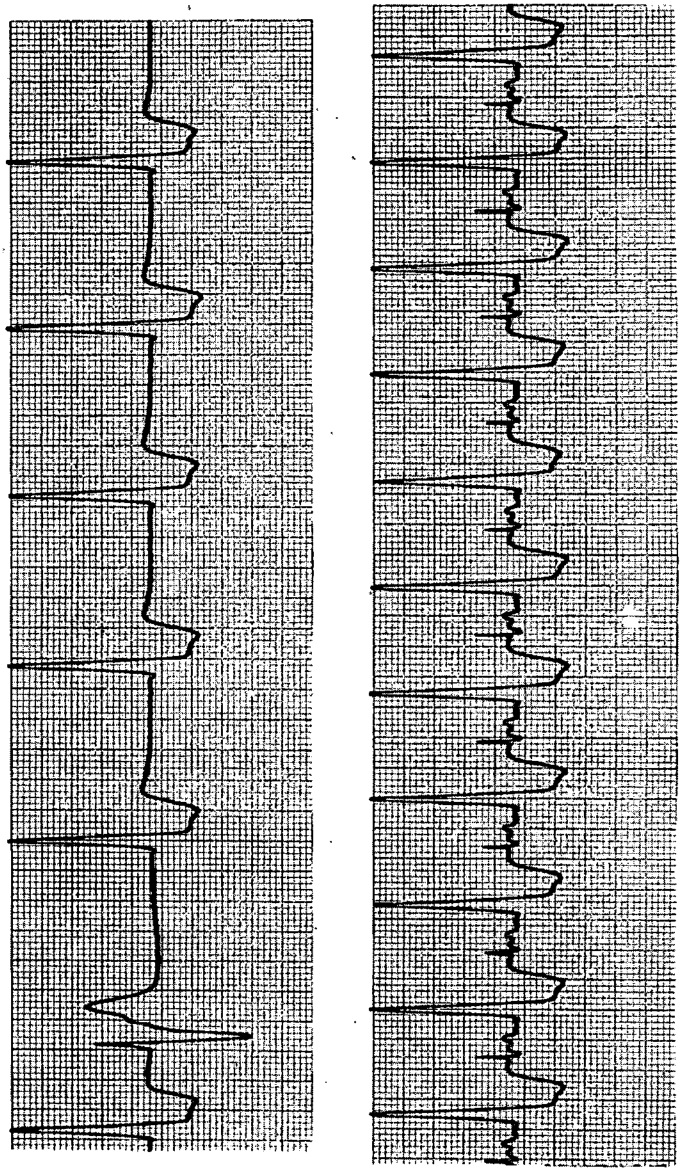

Figure 6. (*Top tracing*) Junctional rhythm with one aberrantly conducted beat. (*Lower tracing*) Restoration of sinus rhythm following atrial pacing. Note the P waves following each atrial pacing spike.

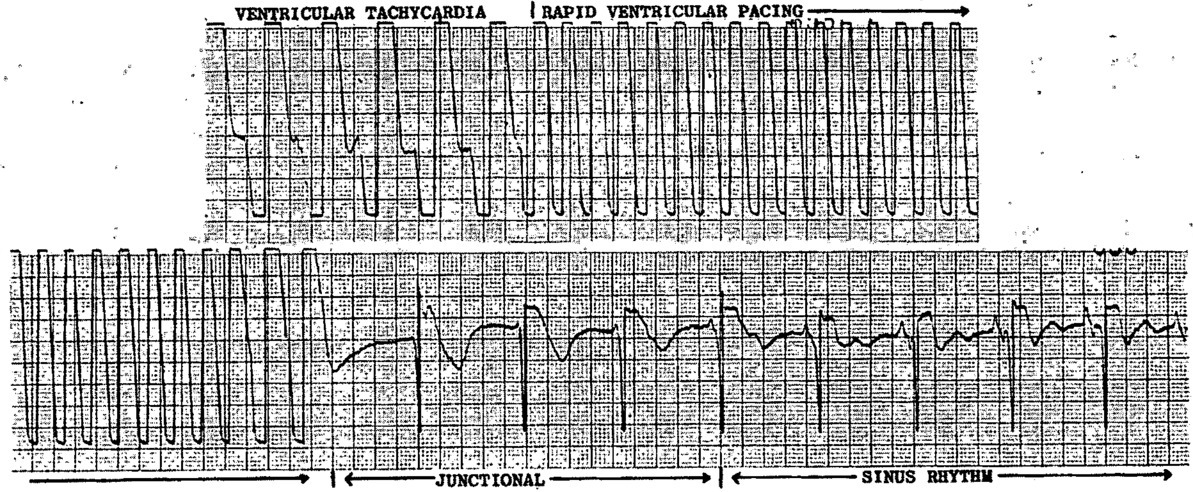

Figure 7. Rapid ventricular pacing converted this patient's ventricular tachycardia to sinus rhythm after three junctional escape beats (the strip is continuous).

rate when attempting to terminate VT. Once pacing has terminated the arrhythmia, begin drug therapy.

Torsade de Pointes

Torsade de pointes' electrocardiographic pattern twists around a central axis. Primary therapy includes stopping antiarrhythmics that prolong the QT interval, correcting electrolyte abnormalities, and assuring a physiologic heart rate. Pacing will not terminate torsade de pointes once it begins; however, atrial pacing is one technique used to prevent the arrhythmia.[10]

Ventricular Fibrillation

Pacing has no role in the termination of a ventricular fibrillation. Defibrillation followed by continuing control with drug administration remains first line therapy.

Atrioventricular Block

Pacing techniques restore rate and sequential contraction sequence when AV block occurs. Patients with a slow sinus rate and first-degree block can be atrially paced to restore a physiologic rate. However, occasionally, patients with first-degree AV block develop second- or third-degree block in response to atrial pacing at faster rates (Fig. 8). In this instance, slowing the pacemaker rate will re-establish 1:1 conduction. AV sequential pacing is necessary if control of the PR interval is desired (normal PR interval = 175 to 200 msec).[39]

Second-degree block with a physiologic ventricular rate does not always require immediate treatment. Ventricular or AV sequential pacing are both suitable. AV sequential pacing maintains the normal AV contraction sequence and therefore at any given rate is associated with the highest possible cardiac output.

Third-degree block is usually associated with excessively slow ventricular rates and requires prompt recognition and treatment. Ventricular pacing with either transvenous or epicardial electrodes is the optimum therapy. Transcutaneous pacing is an important life-saving alternative when epicardial electrodes are not available. When feasible, transcutaneous pacing should be replaced with transvenous because transcutaneous pacing is sometimes associated with burning at the electrode site. When atrial electrodes are also available, first establish ventricular pacing, then use sequential pacing to restore atrial kick and increase the cardiac output and blood pressure.

THE AUTOMATIC DEFIBRILLATOR

Although the idea of electrical defibrillation of a patient in ventricular fibrillation is old, the concept of implanting the defibrillator is quite new. First-generation implantable devices defibrillated patients but did not sense or respond to VT. The newer devices sense VT or fibrillation and electrically react to each arrhythmia.

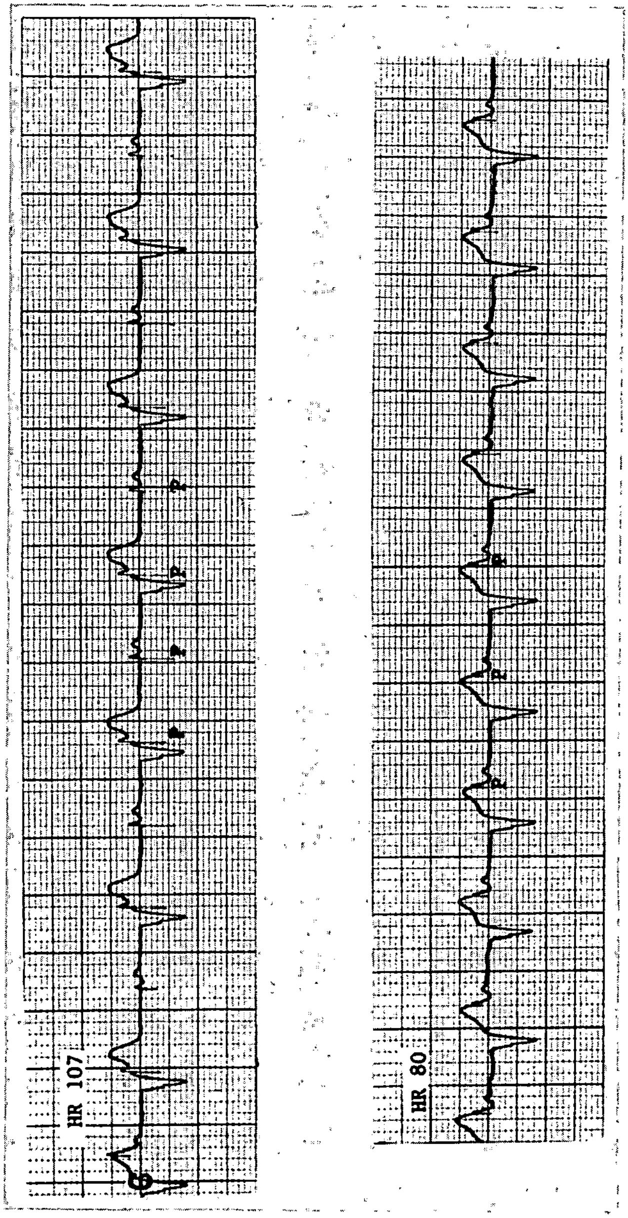

Figure 8. Note that at a higher atrial pacing rate (107, *top tracing*), the patient develops second-degree AV block that resolves by lowering the pacing rate (80, *bottom tracing*). The first-degree block continues at the slower pacing rate. If the patient develops junctional escape beats at a lower pacing rate, then change to sequential pacing. The letter P denotes the atrial pacing impulse and the P wave.

The units sense heart rate and probability density function (PDF).[32] The PDF analyzes the time that the ECG is away from baseline. The normal ECG has several prolonged periods on the baseline. These periods include portions of the PR interval, ST segment, and TP segment. There is minimal baseline stability during ventricular fibrillation. The automatic implantable cardioverter defibrillator (AICD) responds to rate alone or to rate and PDF. The rate-related AICD could cardiovert any rhythm, such as an SVT that has a rate greater than 155. The rate/PDF AICD is more sensitive in that it analyzes rate and QRS configuration to distinguish SVT and VT.

The AICD requires up to 15 seconds to sense the arrhythmia and begin charging. The charge also requires up to 15 seconds, so that the patient could experience VT or VF for 30 seconds before the AICD delivers its first shock. The AICD delivers the second, third, and fourth shocks of approximately 25 J if R waves do not return to the ECG. After the fourth shock, the AICD stops functioning. If a rhythm with R waves occurs after one of the shocks and VF develops again, then the AICD re-initiates its series of four shocks.

AICD Implantation

These critically ill patients are generally suffering from ischemic heart disease. When scheduled for AICD implantation, the patient's antiarrhythmic medications are stopped. The patient therefore enters the operating room without benefit of therapy specific for the arrhythmias and exits the operating room without the benefit of myocardial revascularization. During implantation, the heart is retracted to facilitate the positioning of several electrodes. These unavoidable surgical manipulations decrease preload, cardiac output, and blood pressure with possible ischemic consequences. When testing the device, myocardial ischemia may develop. The patient undergoes rapid ventricular pacing in order to induce VT or VF (Fig. 9). During this period, obviously the cardiac output falls to zero. Commonly, ventricular failure occurs that may require prompt treatment with inotropes and vasodilators.

The AICD requires placement of four electrodes. One large stimulating electrode is placed along the right lateral border of the heart and determines electrocardiographic morphology. A large ground electrode is placed along the heart's left lateral aspect. Two screw-in electrodes located at the apex determine the heart rate. The testing procedure requires initiation of ventricular tachycardia on two separate occasions. The first test is performed with an external device evaluating electrode function. The second test occurs after AICD implantation so that it evaluates the function of the generator. If the electrodes do not function transthoracic defibrillation is necessary. Partially close the chest to assure that this impulse can reach the myocardium. The AICD is programmed off after the testing procedures, therefore the patient remains at risk to develop ventricular arrhythmias. The cardiologist will activate the AICD about 5 days after surgery after performing electrophysiologic tests.

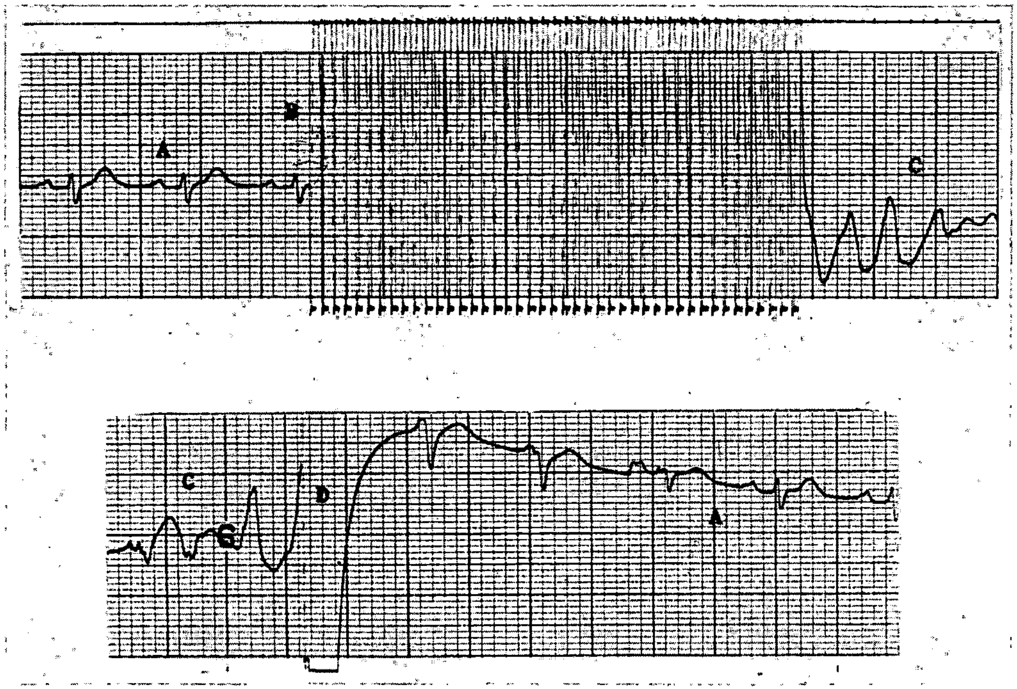

Figure 9. AICD testing occurs in the operating room before chest closure. A, sinus rhythm; B, begin rapid ventricular stimulation to induce fibrillation; C, ventricular fibrillation induced; D, AICD discharge after sensing and charging; A, return to sinus rhythm after AICD defibrillation.

The AICD Patient Scheduled for General Surgery

AICD patients scheduled for general surgery require special consultation with the cardiologist to adjust the antiarrhythmic drug regimen and to deactivate the AICD. As always, the anesthetic management and monitoring must be tailored to the patient's needs and the surgical demands.

The electrocautery could initiate a discharge from an active generator; therefore, deactivate the AICD before surgery. Deactivate the generator by moving the magnet perpendicular to the generator until the magnet lies on the skin over the upper right area of the generator. R-wave synchronous tones will be heard for 30 seconds and indicate that the generator is active. These pulsed tones will change to a continuous tone when the generator becomes inactive. Always use the specific magnet made for the AICD. Removing the magnet from the active generator before the continuous tone occurs evokes the magnet test. The cardiologist uses this test to evaluate the generator's function. During the magnet test the AICD discharges not into the patient, but into the generator. This test discharge is one less clinical cardioversion available to the patient. To reactivate the AICD after surgery, once again place the magnet over the upper right area of the generator. The continuous tone signifying an inactive generator will change to irregular pulsed tones in 30 seconds and finally to R-wave synchronous tones. Remove the magnet in perpendicular fashion and store it away from the patient.

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Diagnosis and Management of Intraoperative Arrhythmias

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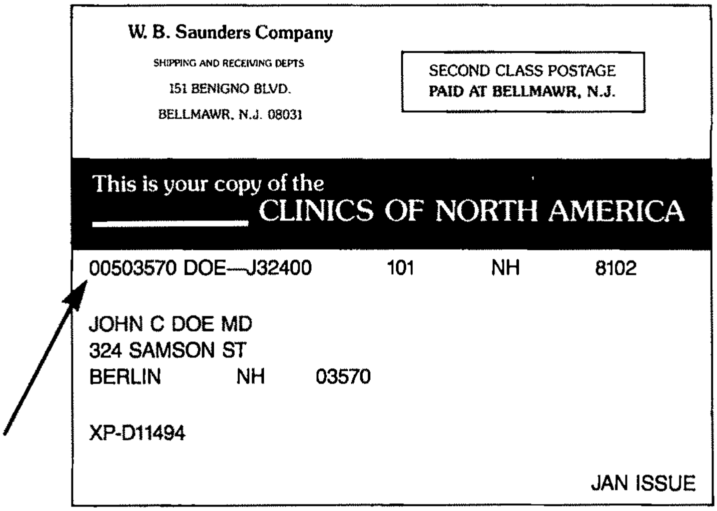

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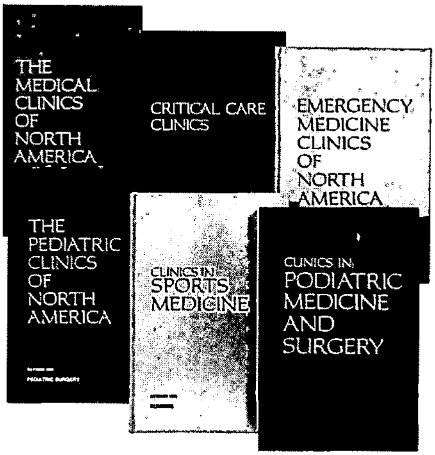
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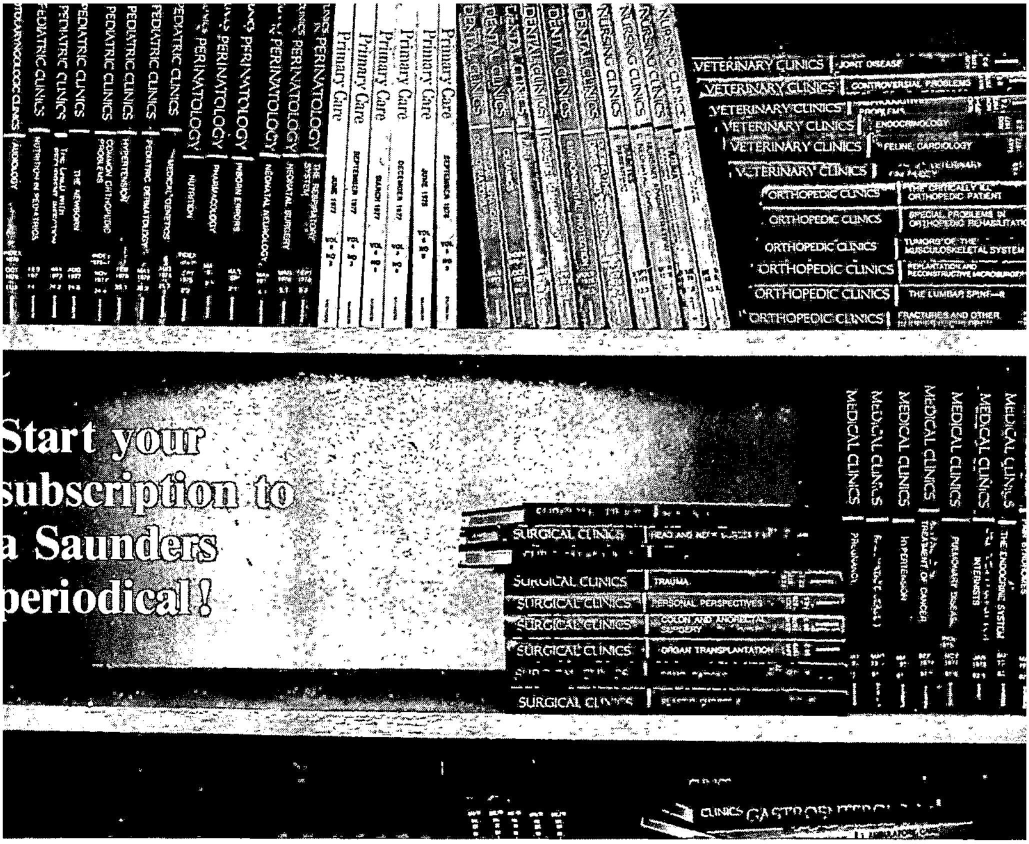

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